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Essential Hypertension in Boy of Two Years of Age. HELEN B. TAUSSIG, M.D., AND DOUGLAS B. REMSEN, M.D..... 183

Observations on Reproduction in the Chimpanzee. A. H. SCHULTZ AND F. F. SNYDER..... 193

Syphilitic Aortitis in Childhood and Youth. ROBERT F. NORRIS, M.D..... 206

Subacute Streptococcus Viridans Septicemia. LOUIS HAMMAN, M.D., AND WILLIAM F. RIENHOFF, JR., M.D..... 219

Rupture of a Papillary Muscle in the Heart as a Cause of Sudden Death. RALPH R. STEVENSON AND WILLIAM J. TURNER..... 235

Book Reviews..... 243

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ESSENTIAL HYPERTENSION IN BOY OF TWO YEARS OF AGE

HELEN B. TAUSSIG, M.D., AND DOUGLAS B. REMSEN, M.D.

From the Harriet Lane Home of the Johns Hopkins Hospital and the Departments of Pediatrics and Pathology of the Johns Hopkins School of Medicine

Submitted for publication May 8, 1935

Persistent hypertension of unexplained etiology is comparatively rare. Indeed, in childhood, as Amberg (1), Comby (2), and others have shown, it is usually found to be associated with certain well recognized conditions, such as chronic progressive renal disease, congenital malformation of the kidney, infections of the urinary tract, coarctation of the aorta, adrenal tumors, and endocrine disturbances (pituitary dysfunction or thyroid disturbance), or cerebral tumors and other conditions associated with increased intracranial pressure.

The group of chronic progressive renal disease constitutes by far the largest number of the cases of hypertension in infancy and childhood. At autopsy these cases show pronounced renal lesions; these lesions are usually associated with frank infection or with some congenital malformation of the kidney. Some cases are reported in which the kidneys are scarred and contracted and show arteriolar lesions similar to those seen in young adults (3, 4). In addition to these cases of renal insufficiency, there is another small group of children in whom the kidney function is normal but who do show vascular changes in the eyegrounds. Amberg (1) and Comby (2) have both reported such cases, which, they believe, correspond to those of malignant hypertension reported by Keith, Wagener, and Kernohan (5, 6).

Examples of persistent hypertension for which no explanation is found at autopsy are most unusual. Isaacs (7) reports one instance of what he believes to be true essential hypertension in a man of 31 who showed only slight thickening of the aorta, but as the patient was still living at the time of the report, no final opinion can be expressed.

Acuna and Winocur (8) reported a case of permanent arterial

hypertension in a girl of 12 years who had two cerebral hemorrhages and eyeground changes. At autopsy the kidneys appeared normal. Unfortunately, investigation of the brain in the region of the vasomotor center proved to be impossible on account of the extensive hemorrhages. The development of the chromaffin tissue of the adrenal appeared to be greater than usual.

Siegel and Thomas (9) have reported a case of hypertension in a child of 12 years which they attributed to hyperactivity of the adrenal gland. The child was living at the time of the report so that no final statement could be made.

Hutchison and Moncrieff (10) described a case of a child of 8½ years in which there was headache, drowsiness, convulsions and coma associated with hypertension and cardiac enlargement and a terminal elevation of the non-protein nitrogen to 66 mg. per hundred cubic centimeters. At autopsy the right kidney was three times as large as the left; both showed cloudy swelling but no other abnormality. Microscopically, all of the blood vessels including the small vessels of the brain and kidney were normal.

Holzmann (11) described a case of hypertension in a boy of 4½ years who complained of cold feet. Kidney function was normal, and no evidence of tumor could be found. No statement was made ruling out coarctation of the aorta. Although no explanation was found, as the report was only a clinical one, no final conclusion could be reached concerning the etiology of the hypertension.

Mussliner (12) and Katz (13) have each reported a case of idiopathic hypertrophy of the heart in which the myocardium was normal at autopsy. In both instances one of the parents was found to be suffering from cardiac enlargement and cardiac failure due to hypertension. Both authors postulated that the idiopathic hypertrophy was due to hypertension because of the similarity of the clinical picture in the parent and the child. Unfortunately, in neither case was the infant's blood pressure taken, so that these cases remain a matter of speculation.

In recent years, attention has been directed to the possibility that hypertension may be due to the presence of pressor substances or the absence of depressor substances in the blood. Hoyle (14) has reported a case of hypertension in a girl of 14 in whom all the usual causes of

hypertension were excluded. The urine of the patient, when injected into a cat, was found to contain an adrenalin-like substance which caused an elevation in the blood pressure of the animal. Capps, Ferris, Taylor, and Weiss (15) subsequently reported that a similar reaction can be obtained from the urine of many normal people.

The following case is reported in detail because, although there were minute renal changes and a slight reduction in the phenolsulphonephthalein, there was no adequate explanation for the long-standing hypertension, *i.e.*, no coarctation of the aorta, no tumors, and no abnormality in any of the organs except the kidney. Furthermore, the lesions in the kidney were quite different from the arteriolar and glomerular changes usually associated with hypertension.

REPORT OF CASE

W. T. (HLH No. 76668) a colored boy of 1 year and 11 months, was first brought to the Harriet Lane Home on March 9, 1932, suffering from a cold and a cough of three weeks' duration.

Family history non-contributory. Both parents living and well. There was no history of lues or hypertension. The patient was the fourth child of five normal full-term pregnancies. The blood Wassermann in both parents was negative, and their blood pressures (taken subsequently) were normal.

Past history: Birth was normal; the birth weight was unknown. The child was a thin infant and did not gain well for the first seven months. He was breast fed for two weeks; then given Eagle Brand condensed milk; and finally, at 7 months, "Infant Diet" and solid foods were added. From 7 months to 1 year of age, he was given orange juice and cod liver oil. The child had had no contagious diseases. His development was normal. There was no history of lead poisoning nor of eating paint.

Present illness: The mother dated the onset of the present illness to three weeks before admission when the child developed a cold and a cough and began to breathe heavily. The appetite was poor. There was frequent vomiting, but the bowels were regular and the stools normal.

Physical examination: Temperature 36.2°C. Pulse 140. Respiratory rate, 40. Weight, 11.3 kg. Height 81 cm. The general appearance was that of an obviously ill boy with rapid grunting breathing. The *skin* was negative. No general glandular enlargement. The *head* was of normal contour. The *eyes* showed a definite icteric tint. The *pupils* were normal. The *fundi* were negative. The *ears* and *nose* were essentially negative. *Teeth* in good condition. *Gums* normal. *Throat* moderately injected. *Tonsils* enlarged and red. The *neck* showed no rigidity. *Thyroid* not enlarged. The *chest* was symmetrical and showed no deformity. The respirations were shallow, regular, and rapid—40 per

minute. The *lungs* were hyperresonant, but there were no abnormal changes in breath sounds and no râles. The *heart* was markedly enlarged. The point of maximal impulse was in the fifth interspace, 6.75 cm. from the mid-sternal line. The rate was rapid—140 per minute. There was a gallop rhythm. The aortic second sound and the pulmonic second were both loud. There was a very faint apical systolic murmur which was not transmitted. A teleoroentgenogram showed that the heart shadow extended 3.5 cm. to the right and 7.5 cm. to the left. Total internal diameter of the chest, 16.1 cm. The *blood pressure* was 124 systolic and 92 diastolic. The *liver* extended 2½ to 3 fingerbreadths below the costal margin. The *spleen* was not felt. The *genitalia* were normal. The *extremities* were essentially negative. There was no clubbing, no cyanosis, and no edema. The impression at the time of admission was myocardial failure of unknown etiology.

Laboratory examinations showed the following: Red blood cells 3,890,000; hemoglobin 75 per cent (Sahli); the white blood count varied from 8,000 to 12,000 of which, approximately, 58 per cent were polymorphonuclear cells. The blood smear was normal; there was no sickling of the red blood cells. The *urine* was of a clear straw color; the specific gravity varied between 1.002 and 1.027. There was no sugar. There was a trace of albumin and acetone ++. There was no bile. The microscopic examination was negative; there were no red blood cells, no white blood cells, and no casts. The *blood pressure* was 130 systolic and 100 diastolic in both the arm and the leg. The *blood chemistry* studies showed: non-protein nitrogen, 35 mg. per 100 c.cm., and carbon dioxide-combining power, 46 volumes per cent. The non-protein nitrogen test was repeated in May and found to be 33 mg. per 100 c.cm. The phenolsulphonephthalein was 40 per cent in two hours, and when repeated it was 30 per cent in two hours. Blood calcium was 9.7 mg. per 100 c.cm.; blood phosphorus 5.4 mg. per 100 c.cm. *Blood Wassermann* negative. *Tuberculin* test negative to 0.1 mg. of tuberculin.

Course in hospital. The patient improved greatly in the first twelve hours of rest in bed. The heart action became quieter, and the gallop rhythm disappeared but could be easily elicited on slight exertion. The rate remained rapid. The liver decreased in size so that it extended only 1½ fingerbreadths below the costal margin. The blood pressure remained high in both the arm and the leg.

This improvement was of short duration. One week later, in spite of continued rest in bed, the breathing again became grunting in character. The heart appeared to have increased in size, and the gallop rhythm returned. The liver descended. Digitalis was given with marked symptomatic improvement.

On April 15 digitalis was discontinued. One week later he was found to have a definite pulsus alternans which was detected clinically, and with a sphygmomanometer it was demonstrated that the strong beats came through at 160 and the weak ones at 130 mm. of mercury. The following week the child again developed signs of decompensation, and digitalis was again given. From then on the patient was unable to maintain compensation without digitalis.

The course was one of gradual progressive failure. There were periods of improvement alternating with periods of severe cardiac failure. After each successive break, there was evidence of progressive lowering of the cardiac reserve. The respirations continued to be rapid. The liver remained enlarged. The heart was enormous. A gallop rhythm and pulsus alternans were present most of the time. The blood pressure remained elevated. In September and early October the electrocardiograms showed changes in the T waves similar to those seen in coronary thrombosis. On October 4 chemical studies of the blood showed a non-protein nitrogen of 38.7 mg. per 100 c.cm.; calcium, 8.5 mg.; phosphorus, 5.5 mg.; total chloride, 103 c.cm. of 0.1 N. HCl (the equivalent of 600 mg. per cent of NaCl).

The severest period of decompensation occurred on October 24 at which time he was not only dyspneic and orthopneic but also very edematous. Death seemed imminent. The blood pressure rose to the extreme height of 198 systolic and 135 diastolic. The respirations were 60 per minute. The pulse was 140 per minute. Chemical studies of the blood were repeated and showed: non-protein nitrogen, 33.9 mg. per 100 c.cm.; cholesterol, 194 mg.; carbon dioxide-combining power, 57 volumes per cent; serum protein, 6.0 gm. per cent; albumin-globulin ratio, 0.87. The phenolsulphonephthalein was 55 per cent in two hours (*i.e.*, 15 per cent higher than in May). The eyeground changes were minimal. Capillary studies showed a capillary pressure which was greater than that found in the normal adult.

Salyrgan was given with favorable results. There was prompt and marked diuresis. The edema disappeared. The blood pressure fell to the lowest level observed for months, *i.e.*, 120 systolic and 90 diastolic.

The improvement was only of short duration. The blood pressure rose steadily, and although the patient never again became edematous, the respirations became rapid and the liver engorged.

The patient died suddenly on November 25.

Summary: The positive findings were persistent hypertension, cardiac enlargement, progressive cardiac failure in the presence of a slightly reduced 'phthalein excretion (55 per cent in two hours) and a non-protein nitrogen at the upper limit of normal. The clinical impression was *essential hypertension, cardiac enlargement, and myocardial failure.*

Autopsy report (autopsy by Dr. Remsen): The autopsy, (no. 12876) performed 8 hours after death, showed a well nourished, normally developed, negro boy of 2 years, measuring 95 cm. in length and weighing 14 kg. Slight rigor mortis was present. Aside from a little puffiness about the eyes and slight edema of the lower legs, no other abnormalities were noted. No fluid was found in the abdominal or pleural cavities. The pericardial cavity contained only a normal amount of clear yellow fluid. The thoracic and abdominal organs, including the aorta and its branches, were removed together, in order that the structures of the larger vessels could be examined for anomalies and abnormalities. None were found.

The *heart* was firm and much enlarged for a child of 2 years. It weighed 230 gm. The epicardial surface was smooth. The coronaries stood out promi-

nently but presented no irregularities of structure; they were patent throughout their course. On section the wall of the right ventricle was thickened, measuring in places as much as 6 mm.; the wall of the left ventricle measured 12 mm. in thickness. All four valves were competent. The mitral valve, however, showed a very slight thickening along the left margin. The endocardial lining of the the left ventricle was smooth but slightly thickened. At a point 3 cm. below the aortic orifice, there was a small thrombus projecting from among the trabeculae of the anterior wall. The thrombus was firm and smooth on the surface; on section it appeared translucent, yellow, smooth in the center, and loosely adherent to the heart wall. In this region, the myocardium showed some mottling of the paler areas. No distinct scars were seen except at the apex where the wall was thin; the anterior descending coronary distributed to this area was patent. The aorta was elastic and pale except for occasional thin fatty streaks on its internal surface. The carotid arteries were dissected out and blocks were taken from the bifurcation for examination of the carotid sinus.

The *tracheal nodes* were slightly enlarged, soft, and of a deep pink color. The *ribs* showed normal lines of ossification. The *lungs* both showed partial atelectasis due to the pressure exerted by the enormous heart. They were firm and elastic, and brownish-red in color. On section no definite areas of consolidation were found nor was there any obstruction in the pulmonary circulation. The *liver* weighed 600 gm.; it presented no gross abnormalities. The *spleen* was large and hard. The *pancreas* appeared normal. Both *adrenals* were small.

The *kidneys* were alike. Each weighed between 50 and 60 gm. and measured 6.5 x 4.5 x 3 cm. Both capsules stripped off readily revealing the remains of fetal lobulation. On close examination, the surface appeared to be slightly granular, showing pale minute raised areas and tiny reddish depressions. On section the cortex seemed to be a trifle swollen and the striations indistinct. No hemorrhages were visible. The *pelves* and *ureters* were normal, and so was the *bladder*.

The *brain* showed no gross changes in the meninges, vessels, nor in the brain substance.

Microscopic Notes:

Heart: The sections showed distinct hypertrophy of the myocardial fibers. In one section taken near the apex, there was slight diffuse scarring. Another section showed a small, well organized thrombus lying between the endocardium and a portion of the papillary muscle. A few fibroblasts were beginning to invade the thrombus. In the adjacent heart muscle, there was a slight, but definite, cellular reaction. The section showing the mitral valve and a branch of the coronary artery appeared normal.

Arteries: In the sections taken from the aorta, the carotids at the bifurcation, the radial and the brachial arteries, the media seemed prominent; aside from this there was nothing unusual. No abnormalities were noted in the sections taken to demonstrate the *carotid bodies*. These were studied with ordinary stains and with a silver stain.

Thymus, thyroid and *parathyroids* showed no lesions. The *ribs* were normal. The *tracheal node* showed the sinuses filled with blood. The *lungs* in one section showed partial atelectasis with a few areas of edema. Another section showed numerous heart-failure cells and slight peribronchial infiltration. The *liver*, aside from slight atrophy of the cells in the central areas, showed no lesions. In the *spleen*, the Malpighian bodies were large with prominent germinal centers. Many of the sinuses were filled with blood. The *pancreas* and the *adrenals* showed no lesions; the arterioles appeared normal. The *stomach*, *ileum*, and *colon* showed no lesions.

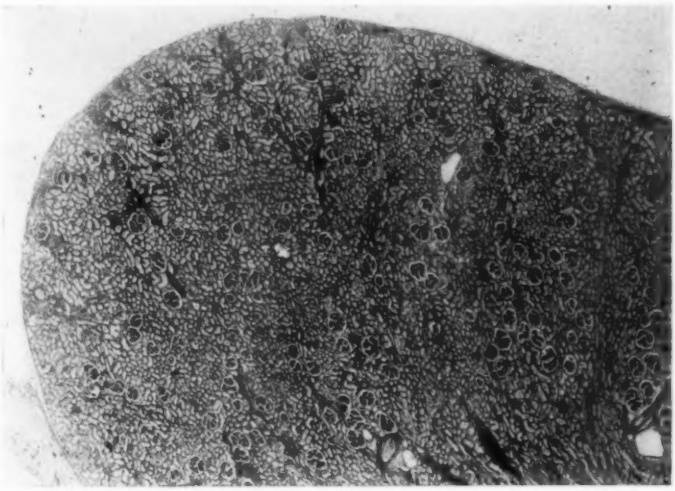

FIG. 1. LOW POWER FIELD OF KIDNEY SHOWING THE SMALL SCARS ALONG THE CORTICAL MARGIN

Kidneys: Sections of each kidney showed similar changes. There were occasional small scars along the cortical margin. These were composed of partially obliterated tubules, slight increase in the connective tissue between the capillaries of the glomeruli, and a few large mononuclear cells, plasma cells, and small round cells. Aside from the possible fibrous thickening of the glomeruli in the areas of slight scarring, no other change could be made out. The basement membrane stain did not show any remarkable thickening. Here and there a minute arteriole was found to contain a hyaline thrombus. This was clearly demonstrated with a fibrin stain. This stain also revealed in one section two or three areas in which a small group of tubules contained colloid droplets in the epithelium. There was an occasional tubule containing albumin, and in one or two of the contracted

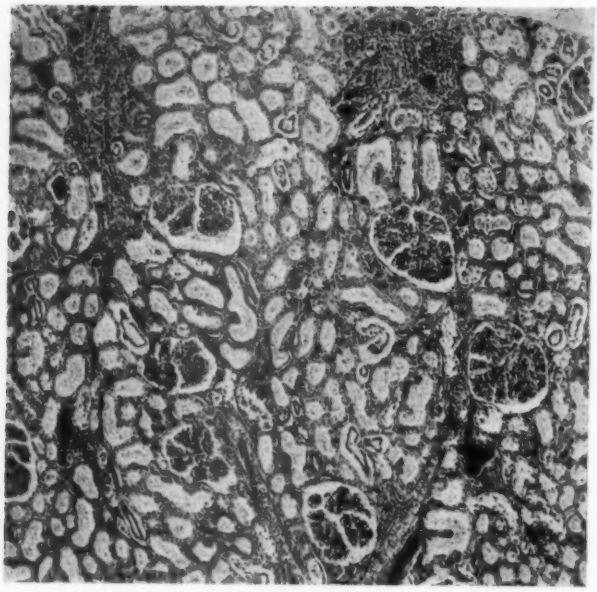

FIG. 2. HIGHER MAGNIFICATION SHOWING THE LOCATION OF THE SCARRED AREAS IN THE KIDNEY TISSUE

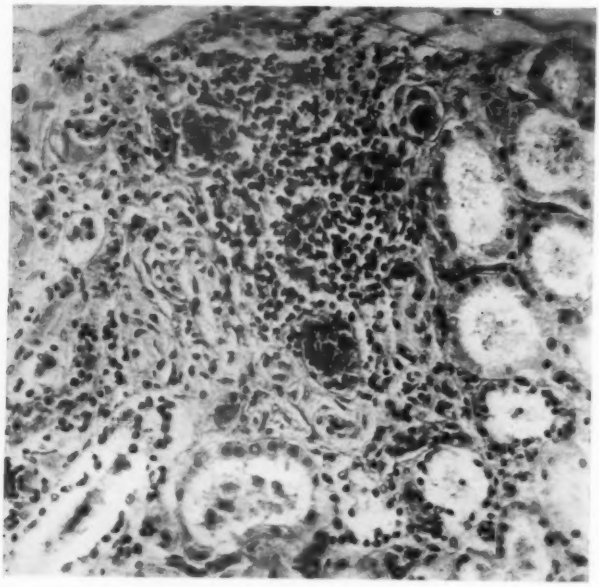

FIG. 3. HIGH POWER MICROPHOTOGRAPH OF THE SCARRED AREA SHOWN IN FIGURE 2

tubules adjacent to the minute scarred areas hyaline casts were found. A fat stain in the kidney revealed small droplets of fat in many of the tubular cells. There were no changes found in the arteries or the arterioles.

The *bladder* showed no lesions. The *testes* appeared normal.

In the *brain*, the basophils, as brought out by Mann's stain, appeared somewhat increased in number toward the marginal surface of the anterior lobe; the eosinophils seemed somewhat concentrated in the central portion. There was slight basophilic invasion of the posterior lobe. The *medulla* showed no lesions.

The final *anatomical diagnosis* was: Cardiac hypertrophy with a small, partially organized mural thrombus and slight scarring of the left ventricular wall. Slight chronic passive congestion of the lungs, the spleen, and the liver. Slight edema of the legs and the face. Partial atelectasis of both lungs. Slight scarring of the kidneys.

Summary: The case is that of a 2-year-old colored boy with hypertension, cardiac enlargement and progressive cardiac failure. The hypertension was persistent throughout the eight months during which the child was under observation. The fact that, when first seen, he showed marked cardiac enlargement and cardiac failure indicated that the hypertension had already existed for several months. The clinical evidence of renal involvement consisted in a non-protein nitrogen varying between 38.7 and 33.9 mg. per 100 c.cm. and phenolsulphonephthalein varying between 30 and 55 per cent in two hours. There were no definite changes in the ocular fundi. The cardiac picture was similar to that so frequently seen in adults with long-standing hypertension, *i.e.*, marked cardiac enlargement, pulsus alternans, coronary T waves in the electrocardiogram, and congestive heart failure. The autopsy, even with the examination directed towards an explanation of the long continued hypertension, yielded little, if anything, of a positive nature. All gross anomalies of the arterial system were clearly excluded. There was no evidence of the arteriolar disease so constantly associated with the adult cases of hypertension. The lesions in the kidneys (as shown in the accompanying microphotographs) appeared to be too slight, too widely scattered, and, as a matter of fact, of too recent origin to form the basis for the known duration of the hypertension. The possible rôle of the hypophysis, the carotid sinus, and the medulla can only be a matter of speculation. There is no definite histological basis for such speculation. In conclusion, although the kidneys cannot be con-

sidered entirely normal, this case appears to be one of essential hypertension.

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OBSERVATIONS ON REPRODUCTION IN THE CHIMPANZEE

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INTRODUCTION

In connection with the widespread recent success in breeding captive chimpanzees there have appeared a considerable number of reports dealing with the phenomena of reproduction in this anthropoid ape, which is generally credited as being the nearest relative of man. The essential facts from these scattered reports are brought together in this communication which contains also new observations on adolescence and pregnancy in the Johns Hopkins colony of chimpanzees. Whenever possible, these data are compared with the corresponding information for man on the one side and for the macaque on the other.

Although some of the conclusions to be drawn from such comparisons are tentative, they throw significant light upon such problems as the origin of the substance diagnostic of pregnancy appearing in the maternal urine, the possibilities for individual variations in many features of sexual life, and the phylogenetic relationship between man and some of the other primates as indicated by this physiological evidence.

PUBERTY

First swelling of sexual skin. In the chimpanzee and many of the lower Old World monkeys, in contrast to man, orang-utan and gibbon, the skin of the genital region, beginning with puberty, undergoes profound changes manifested chiefly by periodic swellings (see *e.g.*, Hartman, 1932, for macaque; Zuckerman and Fulton, 1934, for chimpanzee).

In the female Hopkins chimpanzee, Evo, the sex skin became oedematous for the first time when she possessed all her permanent teeth except the third molars, and at the carefully estimated age of 9 years and 1 month (for correlation between dentition and age see Schultz, 1935). This swelling persisted for nearly 8 months, *i.e.*, until a few days before her first menstruation. In the second female Hopkins chimpanzee, Mae, the first sex swelling appeared at a dental age closely corresponding to that in Evo, but, in contrast to that in Evo, this swelling lasted for only about 3 weeks, and has not reappeared at the time of writing, about 5 weeks later. In the third female Hopkins chimpanzee, Pandora, the sex swelling had made its first appearance before the permanent canines had erupted and persisted very pronouncedly for approximately 14 months. Neither Mae nor Pandora has as yet menstruated.

The difficulty of the attempt to correlate the swelling of the sexual skin with the functioning of the generative organs is further illustrated by previous observations on various other chimpanzees. In Dwina (Tinklepaugh, 1933) swelling first appeared at an estimated age of 9 years. Five months later the first menstruation occurred. There were 4 cycles of fluctuation in the amount of swelling during the interval of 5 months. In Cuba (Yerkes, 1935), born in captivity in 1926, swelling first appeared in 1933, at the age of 7 years. Menstruation first occurred about 4 months later. In Kani (Zuckerman and Fulton, 1934) swelling first appeared at an estimated age of 7 years, and irregular fluctuations in amount of swelling were noted during the subsequent year. In the animal "S" (Zuckerman, 1930) swelling was noted 2 years before the onset of menstruation. It is evident from these collected observations that the interval between the appearance of the first sex swelling and the first menstruation, as well as the occurrence and duration of periodic changes in the amount of swelling, can vary individually to a surprising degree.

For the macaque, which has been extensively studied, Hartman (1932) has pointed out that the swelling of the sex skin is strictly a phenomenon of adolescence, although not all adolescent animals exhibit it. With regard to the time of onset of the swelling in relation to the appearance of the first uterine bleeding, Dr. Hartman states in a personal communication that he has observed no marked

swelling prior to the onset of menstruation, although slight reddening of the skin of the genital region preceded the menarche in some animals.

First menstruation. The first menstruation of Evo occurred at the estimated age of 9 years and 9 months, and 9 months before the eruption of the lower third molars.

It may be mentioned here that, 2 weeks before the first menstruation of Evo, a striking change in the temperament of this animal was definitely noted. Evo had been accustomed to a thorough monthly examination and measurement for 5½ years and had invariably cooperated in this to a quite unusual extent. It is therefore all the more surprising that, during the examination preceding her first menstruation by 2 weeks, the animal resisted the accustomed procedures in a passive as well as in an active manner.

The onset of menstruation has been observed at various ages in other chimpanzees. In Cuba, the first menstruation occurred at the known age of 7 years and 4 months. In Dwina, bleeding first occurred at an estimated age of 9 years (estimated by Schultz, 1935, as less than 8 years). In Boo-Boo (Wyatt and Vevers, 1935) the first menstruation took place at an estimated age of 8 years. Marianne (Fox, 1929) was thought to be about 5 years of age when periodic bleeding began.

In the macaque, menstruation begins on an average at the age of 3 years according to the extensive evidence obtained by Hartman (1932).

In human beings the average age at the beginning of menstruation was 15½ years in a series of 11,500 histories obtained from Berlin inhabitants by Schaeffer (1908). As is well known, this age varies in women considerably according to race, climate and social status.

It is interesting to note from these data that in human beings menstruation does begin in the middle of the resting period in dental eruption, preceding the appearance of the last permanent teeth, the third molars. In the chimpanzee the onset of menstruation can take place at the beginning of the same resting period or even slightly earlier, whereas in the macaque the menarche occurs at a very much earlier dental age.

ADOLESCENCE

Length of the menstrual cycle. The menstrual cycle in Evo was recorded with the following results (1st to 10th cycle in days): 41, 41, 39, 40, 37, 35, 34, 39, 39, 34; average = 37.8 days. The actual duration of bleeding was 2 days for 1st menstruation, 4 days for 2nd, 3 days for 3rd to 9th, and 2 days for 10th and 11th menstruation.

In Dwina, Tinklepaugh found the periodic bleeding to recur every 32 to 36 days and to last 5 to 7 days. In Boo-Boo, Wyatt and Vevers reported a cycle of 27–30 days which was observed over a period of 4 years. In Marianne, Fox stated that menstruation occurred about every month, although an interval as long as 7 weeks was observed at times.

Contrasting with the findings in the chimpanzee, Hartman observed a menstrual cycle in the macaque which averaged 28 days. Young animals, however, tended to be more irregular than the more mature monkeys. Duration of bleeding averaged about 4 days.

In human beings Schröder (1928, p. 169) estimates that the length of the cycle approximates the lunar month in about 80 per cent of the cases and bleeding lasts most frequently 3 to 4 days (p. 173), although a longer duration is common. In one series of 4500 cases, it was found that bleeding persisted 3–4 days in 34%, 5–6 days in 26%, and 7–8 days in 29% of the cases (quoted by Schröder).

One to three days before the onset of menstruation the swelling of the sex skin in Evo disappeared and did not reappear until several days after the cessation of menstrual bleeding. The disappearance is more abrupt and rapid than the reappearance of the swelling.

The findings in Evo are in agreement with the careful observations on Dwina (Tinklepaugh, 1933). This animal showed swelling of the sex skin within 1 or 2 days after cessation of menstruation. The sex skin activity persisted for 23 to 26 days, or to within 3 days or less of the onset of bleeding (which lasted usually 5 to 7 days).

It is significant to find that not only in man but also in the chimpanzee and even in the representative of lower catarrhines, the macaque, the duration of the menstrual cycle can vary to a very considerable extent in different animals and in one and the same individual.

Copulation. A few observations may be recorded here with regard to the sexual relations between chimpanzees. The Hopkins male ape, Dayton, grew up with Evo for a period of approximately 5 years. He appeared to be fully sexually mature for a considerable time before her first menstruation. His dentition became complete very shortly after he had impregnated Evo. About the time of Evo's first menstruation the younger Hopkins female, Pandora, was added to the colony. Dayton had regular and frequent sexual intercourse with Pandora from the start, even though she never menstruated but showed merely pronounced sex swelling throughout the period from her arrival to the present. Dayton did not attempt intercourse with Evo, nor did she solicit it, until her 7th menstrual cycle, or approximately 8 months after her first menstruation. The beginning of their sexual relations at this time may be connected with the fact that prior to it Dayton had been separated from both females for 2 weeks and afterwards had access to Evo only. After once commencing sexual intercourse with Evo, coitus between the two was continued fairly regularly 3 and more times daily for approximately 6 months or for several weeks after she became pregnant. Not until after this time did his active interest in Evo cease and his sexual relations revert exclusively to Pandora, who had been readmitted to his company for 5 months. It is also noteworthy that, according to the records, intercourse between Dayton and Evo did not appear to be markedly influenced by the menstrual cycle of the female. It must be mentioned, however, that Dayton, a large white-skinned male, is an unusually powerful animal who dominates the small, though very active, black-skinned female, who evidently submitted to him many times out of sheer fear.

Adolescent sterility. In the above account of sexual receptivity it is already indicated that, in spite of regular menstruation on the part of the female and abundant coitus on the part of both sexes, no conception took place for a considerable time, namely, for at least 5 months after the first possible exposure and until after the 11th menstrual period, which occurred exactly 1 year after the first menstruation. Evo's estimated age at the time of conception was 10 years and 9 months, or 3 months after her lower third molars had appeared,

and about 8 months before her permanent dentition became completed by the eruption of the upper third molars.

It is interesting to note that in the captive-born chimpanzee, Cuba, (Yerkes, 1935) there occurred a period of infertility which lasted 13 months from the appearance of the first menstrual bleeding until conception. A male of proven fertility had been admitted 3 months before the first menstruation. The age of Cuba at the time of conception was 8 years and 5 months.

In Dwina (Tinklepaugh), a briefer period of infertility was noted, namely 4 months following the first menstruation. At conception her age was approximately 10 years.

In Boo-Boo (Wyatt and Vevers) pregnancy promptly followed coitus, but regular menstruation had been observed for a period of 4 years prior to admittance of the male. Her age was estimated to be 11 years at the time of conception.

In Marianne (Fox), pregnancy occurred about 2 years after the beginning of menstrual cycles, which had recurred regularly. However, a male was not continuously present during this time. Her age was estimated to be $7\frac{1}{2}$ years at the time of conception.

Evidence of infertility in the adolescent chimpanzee is paralleled by findings in the macaque. Hartman observed no pregnancy in these monkeys during the first 2 years after menstruation began. In view of a very high incidence of non-ovulatory menstrual cycles in young animals, it seemed likely that infertility resulted from failure of ovulation. At the time of the first pregnancy, the age was estimated to be about 5 years.

The possibility of a period of infertility in women following the first appearance of menstruation has recently been discussed by Hartman (1931). Conclusive evidence of adolescent sterility in man is difficult to obtain.

These observations, available so far, seem to indicate that the period of so-called adolescent sterility is longest in the most primitive form, the macaque, appreciably shorter in the higher primate, the chimpanzee, and shortest, if indeed existing at all, in man. These differences are all the more significant in view of the fact that the entire growth period is shortest in the macaque (about 7 years), much longer in the chimpanzee (11 years) and longest in man (20 years).

PREGNANCY

Duration. By compiling the data in the literature, which have accumulated during recent years, it is possible to obtain a fairly representative average for the duration of pregnancy in chimpanzees which have given birth to full term fetuses. From the dates published by Zuckerman (1935) for the last menstrual period and parturition in 7 apes the following gestation periods (menstrual age in days) can be obtained: 264, 263, 233, 242, 232, 278, 241. Additional data have been recorded by Tinklepaugh (1933): 264 days (246 days conception age); Yerkes (1934): approximately 228 days (210 days conception age); Yerkes (1935): approximately 263 days (245 days conception age): and Wyatt and Vevers (1935): 254 days. The average of these eleven records equals 251 days from onset of the last menstruation to parturition. This average is very much closer to that for man than to that for the macaque. The former is usually given as 280 days, the latter has been obtained by Hartman as equal to 163 days (conception age) to which must be added approximately 14 days to obtain the average menstrual age of 178 days.

Urine test. The discovery by Aschheim and Zondek (1928) in the urine of man of a substance previously unsuspected has made available a new method for the comparison of man with other species. Numerous investigations have failed to reveal this substance in the urine of animals other than higher primates, although its presence has been noted in the blood of certain *Equidae* (Catchpole, Cole, and Pearson, 1935). It has not been possible to demonstrate this substance in macaques (Snyder and Wislocki, 1931). In the chimpanzee (Zuckerman, 1935) and orang-utan (Zondek, 1931) this material has been noted during pregnancy, although by no means invariably present, as has been found to be the case for man.

The following observations have been undertaken in an attempt to determine whether the presence or absence of this substance in the urine of the chimpanzee is related to the stage of pregnancy at the time of examination. Preliminary observations were made possible through the courtesy of Dr. Tinklepaugh and Prof. Yerkes of the Yale Anthropoid Experiment Station, Orange Park, Florida, through whom were obtained urine samples from 3 different chimpanzees.

Only in the case of the Hopkins female, Evo, was it possible, however, to obtain urine from a single animal at various stages of gestation.

In the present investigation the substance in the urine is defined by its effect on the ovary of the mature rabbit, namely, the induction of ovulation. Previous workers have employed the mouse or rat test as described by Zondek.

The observations are summarized in table 1. In the 4 animals investigated at various stages of pregnancy from 95 days to 180

TABLE 1

Data of rabbit test on urine of chimpanzees at different stages of pregnancy

STAGE OF PREGNANCY, DAYS AFTER ONSET OF LAST MENSTRUATION	AMOUNT OF URINE INJECTED INTO EACH RABBIT (CC.)	NUMBER OF RABBITS USED	OVARIES	PARTURITION, DAYS AFTER ONSET OF LAST MENSTRUATION	CHIMP.	REMARKS
95	5	1	Ovulation	196	*Evo*	Hopkins colony
100	10	2	Ovulation	263	*Josie*	Yale colony
	10					
160	10	4	Negative	264	*Pati*	Yale colony. Mouse test, using 3 cc. of urine for each of 5 animals, was negative
	10		Negative			
	10		Negative			
	10		Negative			
166	2	1	Negative	196	*Evo*	Hopkins colony
171	10	1	Negative	196	*Evo*	Hopkins colony
180	10	3	Negative	Pregnant	*No. 6*	Yale colony
	10		Negative			
	10		Negative			

days, there was evidence of an active substance in the urine early in pregnancy, while tests were consistently negative later in pregnancy. A striking physiological difference between early and late pregnancy is revealed. The nearness of man to the chimpanzee, in contrast to the monkey, is reasserted in terms of the ovulation-inducing activity of the urine, since the active substance is found throughout pregnancy in man, is present for a time in the chimpanzee and is lacking in the monkey.

It is to be noted that these particular results are not in complete agreement with the previous findings of Zuckerman (1935), who noted

no constant correlation between the presence of active substance in the urine and the stage of pregnancy, although at least two of the animals were used in both investigations. This discrepancy may be explained, in the opinion of the writers, on the basis of the fact that Zuckerman made use of the difficult mouse test, whereas in the present study the easily recognized ovulation of the rabbit was relied upon.

Amenorrhoea. As in man and the macaque, menstruation ceases at the onset of pregnancy in the chimpanzee. There are, however, indications, of uncertain reliability, that in rare instances menstruation may recur during the first part of pregnancy in chimpanzees (*e.g.*, von Allesch, 1921; Montané, 1928; Clarke, 1934). Tinklepaugh (1933) first called attention to the fact that sex swelling continues to manifest cyclic changes after the onset of pregnancy. In Evo genital swelling persisted from a few days after her last menstruation to 22 days after that date or to a short time after conception had probably occurred. Three days later this genital swelling reappeared and was present for approximately 5 weeks without ever having reached the extreme stage usually acquired before pregnancy. Two months after the approximate date of conception the sex swelling had completely disappeared and did not develop again throughout her pregnancy. In Boo-Boo (Wyatt and Vevers, 1935) no cycles of swelling were noted during pregnancy, although present before this time.

During the latter part of the third month of pregnancy, Evo's nipples became slightly enlarged and firmer. During the 6th month Evo was observed repeatedly to palpate and lick her nipples. Her abdomen had become enlarged, as could be determined unquestionably by the fact that she could no longer pass through a doorway which had been built particularly to admit the females but exclude the larger male. During the 5th month of pregnancy Evo seemed to feel fetal movements as indicated by the circumstance that, contrary to ever before, she would plainly act as if searching for imaginary insects in her abdominal fur (and nowhere else). This "searching" occurred at irregular intervals, started very suddenly and ended just as quickly a few seconds later.

At about this time her general behavior was slightly more sedate and a good deal more gentle than at any time before.

Complications of pregnancy. On the 188th day (after the onset of the last menstruation) Evo's excellent health changed abruptly. She was observed to vomit violently during the forenoon, became strikingly less active, and lost her previously enormous appetite. On the following day she refused all food except an orange, was even more lethargic and remained lying listlessly near the hot radiator all day. Again she vomited a small amount of dark, mucoid matter in the forenoon. This strikingly unusual behavior speaks plainly for a sudden and severe illness. The same history including vomiting was repeated on the third day. The fourth day of her illness brought a marked and rapid improvement. She ate and drank a fair though far from usual amount. Vomiting had ceased, and there was a good deal of spontaneous activity. During the 3 following days she continued to improve in a most encouraging manner, though she still appeared to be rather weak. On the next day, 196th day of pregnancy, early in the morning Evo was observed to give birth spontaneously to a stillborn fetus presenting by the head. Extrusion of the placenta followed immediately. There was no profuse bleeding. The mother severed the cord by biting it through close to the body of the fetus. She made no attempt to eat the placenta, and carried her dead baby in her groin, refusing frantically to give it up. Judging by the flabby condition of the fetus (jaw dropped open and limbs dangling down) yet complete absence of any excoriation, it can be assumed that the fetus had died approximately 5 days before its expulsion, resulting in a menstrual age of 191 days. This estimate is strongly supported by the weight of the fetus (1000 gm.), its sitting height (250 mm.), the state of ossification of its skeleton, the pigmentation of the skin, and the amount and distribution of hair, in comparison with the exactly corresponding conditions in another chimpanzee fetus (described as No. 2, Schultz 1933), known to have been 189 days old.

The placenta expelled by Evo weighed 169 gm. and the umbilical cord measured without stretching 582 mm.

As far as is possible to decide on the basis of this unusual history, it seems probable that the mother's illness may have resulted from toxemia of pregnancy or possibly from an infection such as pyelitis.

It is especially interesting to note in the ape complications of late pregnancy so strikingly similar to those known to occur in man.

It may be added that the maternal animal made a rapid, complete recovery following parturition.

Chimpanzees have been observed during labor, but the duration of parturition has been difficult to determine. Cuba, a young primipara, was seen 1 hour and 10 minutes before giving birth to a full-term, living offspring, but it was not recognized that this animal was in labor. The placenta was promptly expelled and devoured. In Boo-Boo, also a primipara, labor was recognized 5 hrs. before expulsion of a living term fetus. The placenta was expelled after a delay of 31 hours. In Marianne, also a primipara, labor was noted 2½ hours before delivery of a living term fetus. The placenta was expelled within 10 minutes, but was not devoured.

Complications have been frequent, especially in view of the few animals observed. Dwina died 15 days *postpartum*, apparently as a result of puerperal infection, although labor was spontaneous (Tinklepaugh, 1932). Suzette (Blair, 1920) appeared drowsy for several days following delivery and had fever. Cuba had a post-partum hemorrhage. Boo-Boo failed to expel the placenta for 31 hours after the birth of the fetus, although the length of time the placenta remained in the vagina was not determined.

SUMMARY

Owing to the fragmentary nature of some of the information available so far, it is not profitable to summarize the varied data recorded in this brief paper. It can be definitely concluded, however, that many of the phenomena, appertaining to reproduction, vary individually to as marked an extent in the chimpanzee as in man. In the light of present experience it appears that in general the chimpanzee stands between man and the macaque in regard to the conditions of reproduction. In some features, such as sex swelling, adolescent sterility, and age of first menstruation and of first conception, the chimpanzee resembles the macaque more closely than it resembles man, whereas in others, such as duration of pregnancy, nature of pregnancy urine, and frequency of complications related to pregnancy, the difference between chimpanzee and man is smaller than that be-

tween the former and macaque. In regard to still other features, such as the length of the menstrual cycle, man and macaque are more closely alike than either of the two and chimpanzee.

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SYPHILITIC AORTITIS IN CHILDHOOD AND YOUTH

Report of Two Cases With Sudden Death

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There has always been considerable interest in the occurrence of syphilitic aortitis in young people. Numerous reports of such cases occurring clinically have appeared in the literature, but these cases have always been open to the criticism that the diagnosis was not verified by autopsy. On the other hand, there are comparatively few necropsy reports of syphilitic aortitis in children and adolescents. The discussion in these cases has largely been concerned with the possibility that the lesions were manifestations of congenital syphilis, either because the age of the patients has made the chance of an acquired lesion seem unlikely, or because there have been, in addition to aortitis, manifest lesions of congenital syphilis.

The literature on this subject was thoroughly reviewed in 1930 by Schulte (1) and in 1932 by McDonald (2). The latter author could find but 7 cases with autopsy findings previously reported. To these he added a case of his own. This patient was a boy, aged 9, with interstitial keratitis. His father had been treated for syphilis for six years and his mother was known to have had several stillbirths. The patient was treated with arsenicals for some seven weeks with improvement of his eye condition, but died of acute yellow atrophy of the liver. At autopsy, besides the acute liver necrosis, there was an incidental finding of syphilitic aortitis which did not involve the coronary ostia or the aortic valve. There were no other manifestations of congenital syphilis.

In 1934, McDonald (3) reported eleven more cases of syphilitic aortitis in young adults, four of which he likewise considered to have had a congenital etiology. It is extremely doubtful that the re-

mainder were of congenital origin. Of those cases in which there is evidence in favor of the diagnosis of congenital syphilis, one was in a young man, aged 21 years, who collapsed while riding a bicycle. He died in a very few minutes. At autopsy, he was found to have a syphilitic aortitis with marked narrowing of the coronary orifices and slight thickening of the right aortic cusp. There was no marked scarring of the myocardium. There were apparently no other syphilitic lesions. The sister, aged 19 years, on hearing the news of her brother's death, collapsed and died almost immediately. She, too, showed a syphilitic aortitis with marked stenosis of the coronary orifices. Since the father was a known tabetic, it was thought that these lesions were of congenital origin. Another case was that of a man, aged 21 years, who died of bronchopneumonia. He had been treated for interstitial keratitis five years before. His teeth were described as of the Hutchinsonian type and the Wassermann reaction was positive. There was a syphilitic aortitis at autopsy which did not involve the aortic valve or coronary orifices. There were, however, fresh vegetations on the mitral and aortic valves, which were thought to be rheumatic, although no Aschoff bodies were found in the myocardium. Finally, a single girl, aged 19 years, died with a diagnosis of exfoliative dermatitis. No Wassermann reaction was reported. There was a distinct saddle-shaped nose and, in addition, scars below the nostrils and on the lower lip, and probable Hutchinsonian teeth. Syphilitic aortitis with narrowing of the coronary orifices and thickening of the aortic cusps was found at autopsy.

Because of the paucity of autopsy material in the literature, the following two unusual cases of syphilitic aortitis in young people are reported.

CASE 1

Clinical History: M. C., a colored girl, 9 years of age, was admitted to the Johns Hopkins Hospital on January 14th, 1919. The patient had been well until four days before, when she complained of severe abdominal pain in the right lower quadrant. The pain became generalized in the abdomen and the patient vomited on several occasions. She had been born by a normal delivery and was the last of seventeen pregnancies. There were, however, only seven children living. The mother's first two pregnancies had resulted in stillbirths. Of the remaining eight pregnancies, the children were all born alive, but seven died as young babies of undetermined causes. The mother herself was living and well

at 48 years of age. The father, who was 56 years old, was recovering from a right-sided paralysis. *On admission*, the child was well developed and well nourished. She was semiconscious. Her respirations were rapid and grunting. The temperature was normal. Except for a large tender liver which extended four fingers' breadth below the costal margin, no abnormalities were found on physical examination. Later in the day an X-ray of the chest showed an enlarged heart and possible consolidation of the lower lobe of the right lung. She lapsed into coma and died early the next morning, January 15th. The blood Wassermann reaction was positive. There was a moderate anaemia and a slight leucocytosis. The blood culture was sterile. The other laboratory data were irrelevant. The lack of fever was commented upon clinically; the temperature rose only to 100°F. just before death.

Autopsy (*No. 5792*). A partial autopsy was performed thirteen hours after death. *Anatomical Diagnosis:* Syphilitic aortitis. Stenosis of mouth of each coronary artery. Small focal necroses in myocardium. Probable aortic insufficiency. Focal cellular infiltrations in the liver. Pulmonary oedema; hydrothorax; hydropericardium. Fibrous pleural adhesions.

Body: The body was that of a negro child, weighing 22.5 kilograms and measuring 105 cm. in length. Over the abdomen and on one leg were a few small spots in which the pigment was lacking but without gross evidence of scarring. No abnormalities of the bones were observed. Sections of the skin lesions and of the bones were not made. There were no other external lesions. There was a small amount of straw-colored fluid in each pleural cavity. The lungs on section were oedematous and only partially air-containing, especially at the base of the right lower lobe. The liver weighed 640 grams and showed evidence of passive congestion as well. The remaining organs presented no gross abnormalities.

Heart and Aorta: The pericardium appeared to be normal. There seemed to be a slightly increased amount of straw-colored fluid in the pericardial cavity. The heart itself was definitely enlarged and weighed 250 grams. On section, no abnormalities of the auricles or ventricles were noted, but the myocardium was flabby. The valves all appeared normal with the exception of the aortic which was said to be thickened at its base. There was also said to be separation of the cusps, which would indicate that the aortic valve was insufficient and would account for the cardiac hypertrophy. The heart is no longer available for study so that the lesions of the aortic valve and aorta cannot be reviewed. The sinuses of Valsalva and the ascending aorta showed a thickened wrinkled intima with dilatation of the lumen. The process stopped abruptly at the beginning of the transverse arch, beyond which the aorta was normal. The orifices of both coronary arteries were said to be distinctly narrowed but not occluded.

Bacterial Culture: Culture from the heart's blood at autopsy showed no growth. Culture from the right lung showed only the usual variety of organisms found postmortem.

Microscopic Lesions: Aorta: In sections of the ascending portion of the aorta, there is a distinct irregular thickening of the intima and numerous areas of peri-

vascular round-cell infiltration in the media, the elastic and muscle fibres of which are broken at these points. The adventitia is thickened and scarred, and here there are also many areas of perivascular round-cell infiltration consisting mainly of small lymphocytes with a few plasma cells. The whole appearance is entirely characteristic of syphilitic aortitis.

Heart: Sections of the left ventricle seem normal except for two or three small areas near the base of the ventricle, a few millimetres beneath the endocardium. Here there is necrosis of the muscle fibres and infiltration with neutrophilic leucocytes.

Other Organs: The lungs show only oedema and patchy small areas of atelectasis. The liver shows evidence of chronic passive congestion with atrophy of the central liver cells. In most of the portal spaces there are collections of small lymphocytes and plasma cells, but there is no scarring nor increase of the periportal connective tissue. The remaining organs show no microscopic lesions.

Levaditi Stains: No spirochaetes were demonstrated by the Levaditi method in sections of the aorta, myocardium, lung, spleen, liver, and kidney.

CASE 2

Clinical History: J. H., a 17 year old white boy, was pulling a cart-load of wood along the street on September 3rd, 1934, when he collapsed and, on arrival in the Accident Room of the Johns Hopkins Hospital, he was in deep coma, cyanotic, and lived for only a few minutes. There was no evidence of an external injury. There was no time for an adequate physical examination. The clinical impression was a subarachnoid haemorrhage from rupture of a congenital aneurysm. The mother at this time said that he had always been well and had never had any severe illness. He had seemed well on the morning of his death and made no complaints. At a later date, she was again interviewed for the purpose of obtaining a more extensive history, but she refused to coöperate and would not allow a specimen of her blood to be taken for a Wassermann test. No laboratory data were obtained on the patient and a Wassermann test was not done.

Autopsy (No. 13,826): An autopsy was done fourteen hours after death. *Anatomical Diagnosis:* Syphilis of aorta, sinuses of Valsalva, and aortic valve. Aortic insufficiency. Stenosis of left and occlusion of right coronary orifices. Extensive scarring of interventricular septum and wall of left ventricle. Atrophy and necrosis of posterior papillary muscle. Slight thickening of mitral valve. Nodular scars in epicardium along coronary arteries. Cardiac hypertrophy and dilatation. Pulmonary oedema. Slight ascites. Fibrous abdominal adhesions. Large spleen and thymus.

Body: The body was that of a well-nourished and well-developed white boy, weighing 51.5 kilograms and measuring 170 cm. in length. There were no external abnormalities and no evidence of trauma. The eyes were normal in appearance. There was no perforation of the nasal septum, and no lesions of the bones were observed or palpated. There were no scars on the external genitalia. There was no oedema or jaundice and no skin lesions were present. On section

the abdominal cavity contained about 250 cc. of clear, straw-colored fluid and there were rather dense old adhesions between the spleen and the parietal peritoneum. The lungs were normal externally and seemed only partially air-containing and were oedematous. The liver weighed 1550 grams but looked normal on section. The spleen weighed 200 grams and likewise seemed normal on the cut surface. The thymus was somewhat large. The remaining organs, including the brain, were normal, grossly.

Heart and Aorta: The pericardium was normal in appearance and its cavity contained between 20 and 25 cc. of clear, straw-colored fluid. The heart was in the normal position. The epicardium showed no signs of inflammation. There were, however, numerous grayish streaks which in some places were bead-like nodules along the coronary vessels. On section, these nodules were seen to be limited to the epicardium. There were no abnormalities of the great vessels and there was no pulmonary embolus. The heart weighed 340 grams; it was distinctly dilated and the wall of the left ventricle was somewhat hypertrophied. The right side of the heart seemed normal and the tricuspid and pulmonary valves were not remarkable. There was slight thickening of the mitral leaflets along the line of closure and some of the chordae tendineae were very slightly thickened and shortened. There was an elevated wrinkled plaque extending out of the sinuses of Valsalva behind the right and left aortic cusps into the root of the aorta where it abruptly stopped after a distance of about 2 cm. The aorta behind the posterior cusp was not involved. The orifice of the right coronary artery was completely occluded by the plaque of scar tissue in the intima of the sinus of Valsalva, but throughout the remainder of the course of the vessel there were no abnormalities. The orifice of the left coronary artery was patent but was distinctly narrowed by a similar process and again the remainder of the artery was normal. The plaque contained areas of calcification on section and its greatest depth was 7 mm. The aortic wall could be followed beneath the plaque, but there were several small grayish opaque areas interrupting the media. The remainder of the aorta was normal.

The aortic cusps were all definitely thickened with rolled margins, and the points of attachment were greatly thickened. The right cusp was extremely distorted and its free margin was fused into the wall of the aorta so that only a small crescent, 5 mm. in width, remained. There was also a small fenestration, 2 mm. in diameter, near the margin of the right cusp on the side adjacent to the posterior cusp. A pouch was thus formed between the right cusp and the sinus of Valsalva. Unfortunately, the photograph does not show this striking change as clearly as could be wished (Fig. 1).

There were two distinct bulges in the wall of the left ventricle. The more pronounced of the two was a bulge of the interventricular septum into the cavity of the left ventricle, near the base of the heart behind the mitral valve. This was in the area supplied by the right coronary artery. There was also a slight thinning of the wall and outward bulging at the apex in the distribution of the left coronary artery. The posterior papillary muscle seemed thin and stretched.

Cross sections of the left ventricle and interventricular septum were made and opaque pale areas of fresh necrosis were seen in places, as well as extensive whitish areas of scarring which appeared to be older (Fig. 2).

Bacterial Culture: Culture of the heart's blood at autopsy revealed the presence of Bacillus coli communior and Staphylococcus albus, which were considered to be of postmortem occurrence and of no significance.

Microscopic Lesions: Aorta: Numerous microscopic sections of the root of the aorta and sinuses of Valsalva reveal a thickened intima with areas of mononuclear infiltration near the internal elastic lamella, the cells of which are lymphocytes and plasma cells. There are, also, areas of calcification. There are areas of rarefaction in the media with breaks in the elastic tissue and round-cell infiltration (Fig. 3). The adventitia is somewhat thickened and there are numerous areas of perivascular round-cell infiltration. The aortic valve is thickened and fibrous; it shows small areas of round-cell infiltration where its free edge is fused with the aorta. Cross sections of the right coronary artery, taken at various levels, show the lumen to be occluded for a short distance from the point of origin. It is filled with a fibrous mass resembling the scar tissue in the intima of the aorta. There is very slight canalization of the mass. The media is intact, but there are a few small collections of lymphocytes in the adventitia.

Heart: The mitral valve shows only a slight fibrous thickening. Nowhere in sections of the left auricle or ventricle are there any lesions suggestive of a rheumatic infection. The muscle fibres of the interventricular septum are extensively atrophied and scarred as is the myocardium of the lateral wall of the left ventricle. Most of the scars seem old, and whole bundles of muscle fibres have been replaced by hyalin connective tissue. In occasional small areas, however, the muscle fibres appear freshly necrotic. The posterior papillary muscle is freshly necrotic and is infiltrated with neutrophilic leucocytes. There is a conspicuous absence of perivascular round-cell infiltration, and evidently the lesions are the result of interference with the blood supply.

Other Organs: The lungs show only extensive pulmonary oedema. In the liver there is slight central atrophy of the liver cells and in many of the periportal spaces there are small collections of mononuclear cells. The spleen appears normal as does the thymus. The remaining organs are, likewise, normal microscopically.

Levaditi Stains: Sections of the aorta and sinuses of Valsalva stained by the Levaditi method do not reveal the presence of spirochaetes.

DISCUSSION

From the gross and microscopic appearance of the aorta in these two cases, it is evident that these are examples of syphilitic aortitis, despite the fact that a Wassermann test was not obtained and that there was a slight thickening of the mitral valve in the second case. There is no conclusive evidence, however, that the infection was of

congenital origin. Maternal Wassermann reactions were not obtained in either case, but even had they been positive, there would still have been the objection that syphilis might have been acquired after the birth of these particular children, although the history of stillbirths and children dying in infancy in the first case is strongly suggestive of syphilis in the mother. There are, furthermore, no other lesions in either case which might suggest congenital syphilis. There is, also, the distinct possibility, however unlikely it may seem, that infection may have been acquired extragenitally at some time after birth. The age of the first patient is decidedly against the acquisition of a primary genital lesion. The absence of any scar on the genitalia in a seventeen year old boy is likewise against a genital portal of entry in the second case. In order to prove without doubt that a given case of syphilitic aortitis represented a congenital infection, it would be necessary to show (1) that the mother unquestionably had syphilis at the time of the child's birth and (2) that the patient had other lesions of congenital syphilis or was known to have had a positive Wassermann reaction at an early age. In McDonald's review of cases previously reported, it is apparent that none of the cases in the literature satisfy all requirements and the same may be said of McDonald's own cases. In view of the great rarity of superinfection, it is reasonable, however, to consider those cases of syphilitic aortitis in the literature with other manifestations of a congenital infection as being congenital in etiology. It is felt, indeed, that these two cases may represent this type of lesion, even though no other lesions of congenital syphilis were present.

One of the arguments, which has commonly been advanced for the congenital origin of a syphilitic aortitis in youth, has been the long time interval between the initial lesion and the onset of symptoms in acquired syphilis. Recently, Maynard and his co-workers (4) state that, in a personal communication, DeGraaf studied 200 dead patients with syphilitic cardiovascular disease, at the Bellevue Hospital in New York. He found that the average interval between the occurrence of the primary lesion and the discovery of heart disease was 22.7 years. In only 10 per cent was the interval less than ten years. Maynard and his associates conducted a study and follow-up on a series of 346 patients who were examined for evidence of cardiovas-

cular involvement as soon as a diagnosis of syphilis was made. In one-quarter of the cases, evidence of cardiovascular syphilis was present within ten years after the primary lesion, but the average interval was twenty years. Moreover, one-quarter complained of symptoms within fourteen years, while the average interval was again twenty years. But there was one case in a negro, aged 35, who had acquired a chancre two years before death with congestive heart failure. And in 8 cases evidence of cardiovascular syphilis was found within three years after the occurrence of the chancre. These authors conclude that syphilitic aortitis begins soon after the initial infection but goes unrecognized until symptoms of aneurysm or cardiac involvement occur. A case (Autopsy No. 3287), in the files, has recently come to our attention. A negro man, aged 25, died of syphilitic aortitis 18 months after the chancre was acquired. There was a large saccular aneurysm of the sinus of Valsalva in which was a fresh thrombus which had apparently occluded one or both coronary orifices. It seems, therefore, not unlikely that a few cases of serious damage to the heart and aorta may occur within one to five or ten years following the initial lesion and that, consequently, young adults with such lesions should not be considered to have congenital syphilis in the absence of other evidence.

The two cases here presented occurred among 14,000 consecutive autopsies at the Johns Hopkins Hospital. They represent an incidence of only 0.014 per cent which seems to correspond very well with the scarcity of cases reported in the literature. There were in all 34 cases of syphilitic aortitis occurring before the age of 30 years among these autopsies, but the youngest of the other patients was 20 years and there was no evidence suggestive of a congenital infection in any of them.

Of interest in the cases reported here was the occurrence of sudden death. In this connection, it should be noted that there was distinct encroachment by the syphilitic process on the orifices of both coronaries in the first case and that the right coronary was completely occluded and the left distinctly narrowed in the second case. That syphilitic aortitis may cause coronary occlusion has long been known. Longcope (5) has discussed the clinical significance of stenosis of the coronary arteries. Scott (6) and Reid (7) have recently discussed

the incidence of the lesions. In 1927, Clawson and Bell (8), in an analysis of 126 cases in adults, found that 25 died suddenly and unexpectedly. In all but one of these narrowing of both left and right coronaries was present. Cannon (9) reported two such cases in 1930 with symptoms of three weeks and three months, respectively. In one, the left coronary orifice was occluded, in the other the right. Pincoffs and Love (10), in 1934, reviewed the subject. They analyzed the cases found among 1000 consecutive autopsies in regard to the clinical symptoms. In 15 cases with stenosis or occlusion of the coronary orifices, the average duration of life after the onset of cardiac symptoms was 4.3 months and none of these patients lived for one year. All but one of them died during their first and only hospital admission. These authors emphasize the importance of such lesions in shortening the life expectancy and in causing sudden death in cases of syphilitic aortitis. It is to be noted that in two of McDonald's cases sudden and spectacular deaths occurred, similar to that of the second case reported here. In the first case, likewise, death was certainly unexpected. Although the condition is admittedly rare, it is clear that sudden death in young people may have such an etiology.

Finally, the extensive necrosis and scarring in the second case, is apparently unusual. Scott (6) noticed in his cases that there was little scarring in the myocardium and believed that this lack of extensive scarring was the result of the slowness in closure of the coronary orifices, which allowed a collateral circulation to be established. Clawson and Bell (8) also found no marked scarring as the result of stenosis or occlusion of the coronary orifices. Martland (11) is at a loss to explain the sudden death in his cases because of the lack of extensive myocardial lesions. Love and Warner (12) believe that the changes in the myocardium in such cases are less pronounced than in cases of arteriosclerosis of the coronaries. Saphir (13), however, in a review on syphilitic myocarditis, states that although many cases of stenosis of the coronary arteries do not show marked lesions of the myocardium, there are instances of syphilitic aortitis showing myocardial infarction, which can be attributed only to constriction of the orifices of the coronary arteries. In the second case reported here such lesions existed. When, however, the heart was opened in

the routine manner, no extensive scarring was visible and none was seen microscopically in the routine sections of the left ventricle. Only after cross sections of the interventricular septum and the left ventricle were made did the extent of the myocardial damage become apparent. It therefore seems entirely probable that some cases with lesions of similar extent have been previously overlooked.

SUMMARY AND CONCLUSIONS

1. Two cases of syphilitic aortitis are presented. One was found in a nine year old girl and another in a boy of seventeen. There is some evidence that the lesions were of congenital origin.

2. These were the only cases suggestive of congenital syphilis of the aorta among 14,000 autopsies at the Johns Hopkins Hospital.

3. That syphilitic aortitis with involvement of the coronary ostia may be, in rare cases, a cause of sudden death in young people has been emphasized.

4. Gross myocardial necrosis and scarring in cases of syphilitic aortitis resulting from stenosis and atresia of the coronary orifices occur occasionally and should be carefully searched for.

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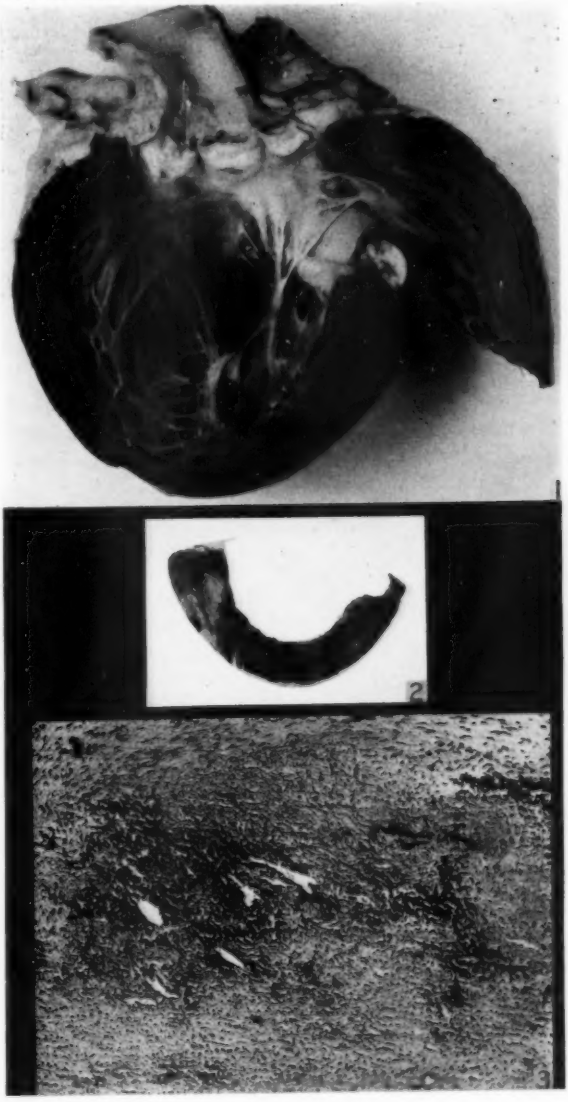
EXPLANATION OF PLATE

(Photographs by Mr. Milton Kougl)

FIG. 1. *Case 2.* Heart showing aortic valve, with aortitis above it.

FIG. 2. *Case 2.* Cross section of the interventricular septum, and part of lateral wall of left ventricle, showing fibrosis of myocardium.

FIG. 3. *Case 2.* Typical lesion in the media of the aorta.



UNIV OF MICH

SUBACUTE STREPTOCOCCUS VIRIDANS SEPTICEMIA

Cured by Excision of an Arteriovenous Aneurysm of the External Iliac Artery and Vein

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On January 21, 1935, Dr. Charles M. Caravati, of Richmond, Virginia, referred to us for examination and diagnosis a young man who had been ill with fever for six months. A brief story of the illness and a summary of the results of the examinations which were made follows:

Unit History No. 60223, Mr. J. A. W., an oil salesman, 35 years of age, entered the Johns Hopkins Hospital, January 21, 1935, complaining of weakness, loss of weight and fever of six months' duration. Before the onset of this illness he had always been a healthy man. He had had several of the minor infectious diseases of childhood. At twenty-six the tonsils had been removed. The only point of interest relative to the recent illness was that at eighteen years of age, May 18, 1918, the patient had accidentally shot himself with a 22 calibre rifle, the bullet penetrating the abdomen just above Poupart's ligament. Immediately after the accident, he was able to walk about fifty yards. He felt a very severe burning sensation in the right leg and bled profusely from the bullet wound. His companions placed a tourniquet around the thigh which stopped the profuse bleeding, but the patient had lost so much blood that he fainted repeatedly while being transported eight miles to the nearest hospital. That evening he was operated upon by Dr. A. M. Willis at the Virginia Hospital in Richmond. After the operation he was told that the bullet had torn a hole in the two large vessels which supply the right leg, and had established an arteriovenous communication between them. An extensive retroperitoneal hemorrhage had occurred. The injury was followed by pronounced swelling of the right leg and for a while the patient was completely disabled. After a few weeks, however, the swelling disappeared and gradually he was able to use the leg more and more until finally, at the end of two months, he could walk about without the use of a cane. During

the next six months occasionally there was some swelling of the ankle in the late afternoon and evening. If the patient exerted himself unusually, cramp-like pains in the leg would come on which, as time progressed, became less pronounced. All symptoms of the injury had disappeared at the end of a year excepting some nocturnal palpitation of the heart, and the consciousness of a vigorous pulsation in the right lower quadrant of the abdomen. There had never been any dilatation of the veins of the right thigh, leg or foot; no changes in the skin; none in the bones by roentgen-ray examination; and the length of the right and left extremities was the same. In 1932 the patient was examined by Dr. Caravati who found no abnormality except the presence of an arteriovenous aneurysm in the lower right quadrant of the abdomen together with moderate enlargement of the heart associated with a rapid pulse, varying from 100 to 120 beats to the minute.

The patient's recent illness dated from July 1934, when he began to feel listless and generally indisposed. His temperature was taken and it was found that each afternoon it rose to about 100°. A little later his appetite failed and in a short time he lost thirty pounds in weight. His symptoms were thought to be the result of a mild infection in the throat. However, although the local manifestations promptly cleared up under treatment, the fever and lassitude persisted. In September he had a number of severe chills, and the possibility of malaria being considered, he was given large doses of quinine. Under this treatment the temperature dropped to a lower level but the general condition did not improve. At the end of September he was so weak and miserable that he went to bed and remained there up to the time of his admission to the hospital.

During the intervening four months the condition had been very thoroughly investigated but no satisfactory diagnosis had been reached. The possibility of amebic dysentery was considered and he was treated with emetine, but without benefit. The fever persisted and he continued to lose weight and strength. Dr. Caravati took charge of the patient in October 1934. At that time the physical examination showed emaciation, pallor, enlargement of the liver and spleen and the presence of the arteriovenous aneurysm. Agglutination tests with strains of Brucella were negative. With the typhoid bacillus, agglutination occurred in a dilution of 1:200. (The patient had received prophylactic typhoid vaccine about seven years before.) On a number of occasions occult blood was found in the stools. The blood showed a mild secondary type of anemia. During October there was a slight leukocytosis, but this soon disappeared and later the leukocyte counts varied from 6,500 to 9,000. Roentgenographic examination of the gastrointestinal tract revealed no abnormality. Fourteen blood cultures had been made and all were reported negative.

Examination. (Made upon admission to the hospital.) Temperature, 101°; pulse, 110; respirations, 22; B.P., systolic 110, diastolic 60.

The patient was an undernourished man with a sallow, anemic complexion. He had evidently lost much weight and his appearance betrayed the marks of prolonged illness. Aside from his weakness and lassitude, he otherwise felt well. He had no pain or other local discomfort. No petechial spots were noted in the

mucous membranes or in the skin. The eyes were normally prominent. The pupils were equal; they reacted actively to light and on accommodation. Inspection of the fundi revealed no abnormality. The teeth were in good condition. The pharynx showed nothing remarkable. The tonsils had been completely removed. There was no enlargement of any of the superficial lymph nodes. The thyroid was of normal size. The chest was rather long and thin, with a narrow costal angle. It was symmetrical and the movements were equal on the two sides. The percussion note over the lungs everywhere was resonant and the breath sounds were vesicular. No râles were heard. The area of cardiac dulness was not enlarged. The heart sounds were clear and of normal quality except for a loud, systolic murmur in the pulmonary area. The pulse was regular, of high amplitude and a little quick, though by no means collapsing in quality. The abdomen was normal in appearance. The walls were soft and relaxed. The edge of the liver could be felt about a fingerbreadth below the costal margin; the border was rounded and the organ of normal consistence. The edge of the spleen was easily felt about a fingerbreadth below the costal margin and was a little tender. In the right lower quadrant there was an intense, continuous thrill on light palpation which was associated with marked excursion of the iliac vessels. On deep palpation the difference between the size of the iliac vessels on the right compared with the normal vessels on the left was very striking. The vessels on the right side were many times larger than on the left. By exercising firm pressure it was possible to obliterate the fistulous opening, thereby causing a cessation of the continuous thrill. It was interesting to note that occlusion of the opening did not bring about perceptible slowing of the pulse rate, indicating that the fistulous communication was probably a small one. A hard, bony-like structure could be felt about the mass which the roentgenogram proved to be the calcified wall of the encysted varicose aneurysm. There was vigorous pulsation in the external iliac artery just above Poupart's ligament and in the femoral artery below. A strong pulsation was easily felt in the dorsalis pedis and posterior tibial arteries. Auscultation over the aneurysm revealed the classical machinery-like to-and-fro bruit, which was markedly diminished in intensity by deep pressure on the upper portion of the external iliac artery. There was no evidence of the development of a collateral circulation about the hip or thigh. There were no varicosities of the veins distal to the point of the fistulous communication. There was no swelling or edema of the soft parts of the thigh, leg or foot. Blood pressure readings:

	Systolic	*Diastolic*
Right arm	120	55
Left arm	125	45
Right thigh	60?	40?
Left thigh	120	55

The skin temperature of the right and left lower extremities was essentially the same. When deep pressure was made over the external iliac artery above the

fistulous communication, there was marked diminution in the blood flow through the femoral artery, but no difference occurred in the appearance of the skin of the right extremity or in its temperature. These observations confirmed the impression that the fistulous communication between the external iliac artery and vein must be a small one. Since there was no change in the temperature or appearance of the skin following deep pressure over the upper part of the external iliac artery, we concluded that the collateral circulation which had developed would be sufficient to prevent serious embarrassment of the blood supply to the extremity should the external iliac artery above the fistula be permanently occluded. The extremities otherwise showed no abnormality, no arthritic manifestations, no clubbing of the fingers. The deep reflexes were normally active.

Laboratory Examinations. Blood Count: Hemoglobin 68%; R.B.C. 3,650,000; W.B.C. 10,000. Differential: Polymorphonuclear neutrophiles, 65%; Lymphocytes, 32%; Monocytes, 3%.

Wassermann Reaction on the blood serum negative.

van den Bergh test negative.

Agglutination tests: Bacillus typhosus positive up to dilution of 1:320. Paratyphoid B. positive up to dilution of 1:320. Paratyphoid A.; Shiga bacillus; Flexner bacillus; Brucella abortus;—all negative.

Blood Cultures: 1/23/35—Streptococcus viridans, 28 colonies per 1 cc. of blood.

1/29/35—Streptococcus viridans, 20 colonies per 1 cc. of blood.

2/6/35—Streptococcus viridans, 49 colonies per 1 cc. of blood.

Urine Culture: No growth.

Urine: Specific gravity ranged from 1.010 to 1.020. Contained neither albumin nor sugar. A few pus cells in the sediment. No red blood corpuscles or casts.

Stool: No gross blood or mucus. Benzidine test negative. Microscopically, some undigested vegetable material, otherwise negative.

Intracutaneous tuberculin test: No reaction.

Roentgenograms: Abdomen: An elliptical body clearly defined by calcified walls overlying sacro-iliac joints. The appearance of this structure is compatible with the diagnosis of arteriovenous aneurysm. A bullet is located opposite the third lumbar vertebra on the right side.

Chest: Increase of the shadows about the middle border of the lungs, due probably to chronic passive congestion. There are no areas of broncho-pneumonia. The heart seems not to be enlarged.

Tele.: M. R. 5.5; M. L. 9; A. 5.5; T. 28.5.

Electrocardiogram: Rate 115. Rhythm sino-auricular. P-R interval 0.14. QRS duration 0.08. Normal sinus rhythm. T I and II upright. T III inverted. Ventricular complexes are sharply defined. Sinus tachycardia.

Discussion. These observations demonstrated conclusively that the patient was ill with Streptococcus viridans septicemia but it was

not clear precisely where the infection was located. It is well known that the Streptococcus viridans often invades the blood stream, sometimes even in large numbers, when there is an acute septic infection, for instance, a severe acute sinusitis. However, under these circumstances the septicemia is brief, for the organisms at once disappear from the blood when the acute infection subsides. Certainly there was nothing in the situation which then held our attention to encourage the hope that the septicemia might be such an acute and transient one. Quite otherwise, for all the facts (the long duration of the illness, the persisting fever, the anemia, the enlargement of the spleen, the repeatedly positive blood cultures) demonstrated that there must be a locus of infection having direct access to the blood stream and continuously discharging bacteria into it. When we observe a clinical picture so characteristic as was this one, we conclude at once that the locus of infection is in the heart because wide experience has taught us that under these circumstances it is nearly always situated in the heart and, save for rare exceptions, upon the valves. Therefore we confidently expect to discover the unmistakable evidence of a valvular lesion, and if the infection has existed for some time, our expectation is seldom disappointed.

The remarkable thing about the present case was that the anticipated evidence of a valvular defect was completely wanting. It may be that the heart was a little enlarged (the measurements of the teleroentgenogram being a trifle more than half the transverse diameter of the chest), but some enlargement might be expected to follow as a result of the circulatory alterations caused by the arteriovenous aneurysm. The heart sounds were clear and of normal quality except that there was a systolic murmur at the pulmonary area. In the presence of anemia and long-continued fever it would be noteworthy did a systolic murmur not appear at the pulmonary area.

Being convinced by repeated examinations that the infection was not located upon the heart valves, two possibilities suggested themselves; (a) that the vegetations were upon the endocardial surface of the chambers of the heart, or (b) that they were situated within the arteriovenous aneurysm. Merely to consider these possibilities was of intense interest, because if reasonable grounds could be found for the belief that the vegetations were within the aneurysm then there existed a prospect of cure.

The occurrence of vegetations upon the endocardial surface of the auricles or ventricles is one of the common observations of the pathologist. Almost every case of subacute bacterial endocarditis will show them, where they have extended directly from the diseased valves or where they have become implanted from the infected valve which, floating to and fro, has rubbed against the endocardial surface. These are familiar observations, but it is another matter to ask whether bacterial vegetations upon the inner surface of the chambers of the heart ever occur as *primary* foci of infection, that is, when there is no valvular disease nor congenital defect. No note of such an occurrence can be found upon the pathological records of the Johns Hopkins Hospital, and both Dr. W. G. MacCallum and his associate Dr. A. R. Rich tell us that they have never seen an instance of it. Therefore, if it ever happens, it must be a great rarity. The fact that no evidence was noticed of embolic phenomena in the general circulation was a point against the infection being located within the left side of the heart.

Unfortunately, the localization of bacterial vegetations within an arteriovenous aneurysm must occur almost as uncommonly as their isolated growth upon the endocardial surface of the heart. A review of the literature failed to disclose a reported example of the condition. Nevertheless, there are many observations which led us to believe from analogy that bacteria might settle and grow within an arteriovenous aneurysm. We refer to the observation of Streptococcus viridans vegetations about the orifice of a patent ductus Botalli or at the site of coarctation of the aorta. We recall also an instance in which bacterial vegetations were situated within an aortic aneurysm. These are clear demonstrations that bacteria often lodge and grow upon the intima of the aorta at points where the vessel is constricted or its walls damaged by disease. From mechanical standpoints an arteriovenous aneurysm is very similar to an open ductus Botalli.

These considerations led us to believe that in the present case, in all probability, the Streptococcus viridans had settled and grown within the arteriovenous aneurysm and from this site of advantage was continuously pouring bacteria directly into the blood stream. Should this be the case then, we reasoned, the septicemia might be

cured and the patient restored to health by excision of the aneurysm. The possibility of gangrene of the leg setting in after ligation of the right external iliac artery was discussed, but upon this point the surgical opinion was entirely reassuring. The Streptococcus viridans is an organism of mild virulence. The view generally held is that it would disappear at once from the blood stream, were there not present a focus from which fresh bacteria are being constantly discharged into the circulation. As we have already said, the sudden flooding of the blood stream with Streptococcus viridans in connection with an acute infection which soon subsides is relatively an innocuous affair.

As matters then stood, the outlook for the patient under conservative treatment was almost hopeless. Study of anatomical specimens teaches that many patients get well from bacterial endocarditis. This anatomical evidence, however, is so glaringly in contrast to clinical experience that we are forced to conclude that most of those who recover must have had such mild symptoms that the infection had passed unrecognized. When the typical clinical manifestations of subacute Streptococcus viridans septicemia are once fully developed recovery does not often follow. Therefore, it was more than likely that the patient would die were no radical measures undertaken.

On the other hand, excision of the arteriovenous aneurysm, should the infection be located there, held out a good prospect of cure. It seemed to us that to perform the operation was risking little in the hope of very great gain. The situation was plainly and fully explained to the patient and his wife. Both enthusiastically chose operation.

Operation. As the illustration (Fig. I) shows, the enormously dilated right common and external iliac arteries, overlain by the right ureter presented in the operation wound. To the left and coursing along the medial side of the external iliac artery, the very much dilated and thin-walled external iliac vein joined with the internal iliac to form on the posterior surface, deep beneath the artery, the common iliac vein. All the visible tributaries of the external iliac vein, *i.e.*, the femoral, deep circumflex iliac and deep epigastric veins were very much dilated. The admixture of arterial and venous blood could readily be seen through the thin walls of the venous channels. The medial edge of the common iliac vein could just be observed along the corresponding margin of the right common iliac artery. Nor-

mally, the vein at this level is covered completely by the artery. The main, dilated portion of the vein also was concealed by the common iliac artery, creating the false impression that the diameter of the common iliac vein was much smaller than that of the external. However, on further dissection this was found not to be the case. Distal to the fistulous opening the external iliac artery was of normal size, or

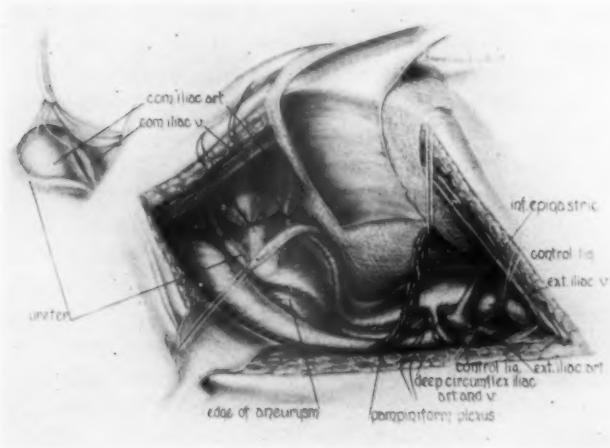

FIG. I. DRAWING, MADE AT TIME OF OPERATION, OF THE DISSECTION OF THE ARTERIOVENOUS ANEURYSM BETWEEN THE EXTERNAL ILIAC ARTERY AND VEIN

Control ligature about external iliac vein was used as a permanent ligature, but the control ligature about the femoral artery was removed, a permanent ligature being placed proximal to the departure of the deep circumflex iliac artery.

perhaps even smaller. On the posterior lateral surface of the artery, lying on the iliacus muscle, was an oval, hard mass, like a hollow chamber, which was connected with the artery and also the vein. One could feel a continuous thrill through its wall. The surrounding adhesions to the artery and the posterior position of the vein and fistula, together with the calcification of the aneurysmal sac, made separation of the individual vessels and an attempt to close the fistulous opening impractical, and because of the size of the vessels,

very dangerous. The common iliac artery and vein therefore were separated by blunt dissection and a control ligature placed about the former. The same procedure was carried out on the external iliac artery and vein. The ureter and overlying pampiniform plexus were removed from the surface of the vessels, which were then exposed throughout their continuity. Permanent ligatures of oiled braided silk were placed at the four cardinal points; *i.e.*, below the fistula, around the external iliac vein distal to the entrance of the deep

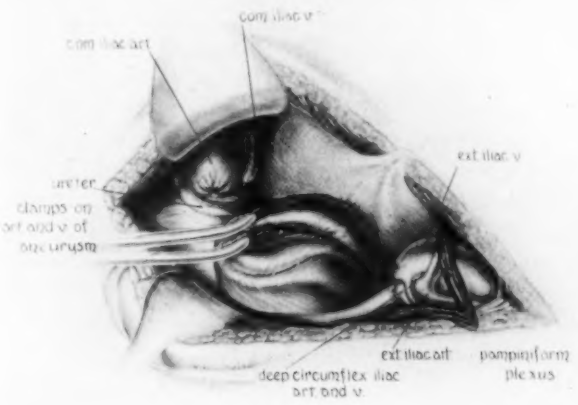

FIG. II. FOUR CARDINAL POINTS HAVE BEEN LIGATED AND ANEURYSM HAS BEEN REMOVED

epigastric and circumflex iliac veins; about the external iliac artery proximal to the departure of the deep circumflex iliac and epigastric arteries; above the fistula about the dilated common iliac vein and artery; and about the internal iliac vein (Fig. I). The control ligatures were removed and after pulling the permanent ligatures home the aneurysm was excised (Fig. II). Some difficulty was experienced in controlling the bleeding from dilated collateral vessels on the posterior surface of the aneurysmal sac, as these vessels were very short, thin-walled and were held patent by the iliacus fascia.

The size of the vessels in the immediate vicinity of the aneurysm would seem to be worthy of record. The right common iliac artery proximal to the fistula was about the size of a normal aorta (Fig. II). The left common iliac artery was perfectly normal in diameter. The portion of the external iliac artery proximal to the fistula was dilated to the same size as the common iliac, and there was some increase, but by no means so great, in the diameter of the internal iliac. The external iliac artery distal to the fistual was of normal size. The deep epigastric and circumflex iliac arteries appeared to be larger than normal. When the permanent ligature about the external iliac artery was pulled home, the femoral artery immediately collapsed, but after fifteen minutes had passed, again it became distended with blood flowing into it by way of the now obviously dilated deep circumflex iliac and epigastric arteries. In other words, in this short space of time the flow of blood in these arteries had completely reversed itself and was now flowing in the direction opposite to normal from their capillary beds through the deep circumflex and epigastric vessels into the distal portion of the external iliac and femoral arteries. This observation was confirmed by a gentle needle prick of the femoral artery which bled readily but not so vigorously as normally it would. The explanation for the selection by the blood flow of the capillaries associated with the deep epigastric and circumflex iliac arteries, instead of proceeding, as it does ordinarily, into their accompanying venous channels, lies probably in pressure differences. The pressure immediately after ligation of the external iliac artery was zero in the arterial tree distal to the ligature. In the veins, however, the pressure was higher, because the deep epigastric and circumflex iliac veins were tributaries of the portion of the external iliac vein forming a part of the aneurysm between the permanent ligatures. Therefore, the patency of the veins and the intravenous pressure were maintained by the blood trapped in the ligated venous side of the aneurysm. The maintenance of the venous pressure forced the blood to the lower area of pressure in the artery and very soon reëstablished the arterial circulation. An explanation is thus afforded for the beneficial effects of ligature of the accompanying vein when ligating the artery Numerous experimental and clinical observations have been accumulated to prove the wisdom of this procedure but heretofore the explanation of the *modus*

operandi of this beneficial venous stasis has not been set forth. The incision was closed according to the usual manner without drainage, *i.e.*, the posterior and anterior peritoneum were sewed with a contin-

FIG. III. PHOTOGRAPH OF ARTERIAL SIDE OF SPECIMEN OF ARTERIOVENOUS ANEURYSM REVEALING THE OPENINGS INTO ENCYSTED ANEURYSMAL CAVITY FILLED WITH VEGETATIONS AND THE PROTRUDING THROMBUS WHICH POINTS CEPHALWARD

Dilated proximal portion of artery shows in upper portion of illustration. The external iliac artery of normal size is shown below. Along the right margin of the artery is the dark calcified wall of the aneurysm. The external iliac vein is on the opposite side lying directly behind the artery.

uous suture of fine silk; the anterior sheath of the rectus muscle and skin with interrupted fine silk sutures. The operation required five and one-half hours but the patient, having lost very little blood, was not in the least shocked.

Description of the specimen. The specimen removed at operation measured 8.5 cm. in length and consisted of a portion of the external iliac artery and vein, a portion of the common iliac vein, and surrounding connective tissue and fat. Attached firmly to the posterior lateral

FIG. IV. PHOTOGRAPH OF THE ARTERIAL SIDE OF THE SPECIMEN SHOWING TWO OPENINGS IN THE ANEURYSMAL SAC BOTH FILLED WITH VEGETATIONS

The dark aneurysmal sac and the small distal portion of the external iliac artery beyond the aneurysm may be seen in the lower portion of the photograph.

surface was an oval calcified mass, measuring 6 cm. by 3.5 cm. by 2.5 cm. The vessels were opened along their anterior surfaces and it was then seen that there was a communicating channel between them and the aneurysmal sac situated about 2.5 cm. from the lower end of the specimen (Fig. III and IV). The opening in the artery and in the vein was 1 cm. in diameter. These openings communicated

with the calcified, oval chamber so that the blood passed from the artery into the aneurysmal sac and then into the vein. This type of abnormal arteriovenous communication should be termed an encysted arteriovenous aneurysm. In addition to the above described aper-

FIG. V. PHOTOMICROGRAPH OF A SECTION OF THE VEGETATIONS PARTIALLY OCCLUDING THE OPENING BETWEEN THE ARTERY AND ANEURYSMAL SAC STAINED TO DEMONSTRATE BACTERIA

Many chains of streptococci are present

tures in the vessel walls there was an additional opening between the artery and vein, about 6 cm. in length, which was in reality almost continuous with the smaller opening. Protruding from the cavity of the aneurysmal sac was a thrombus attached to the arterial wall which pointed cephal-ward in the artery, probably as a result of eddying currents above the point of the fistulous opening where the artery

was constricted (Fig. III). The walls of the vessels were thickened markedly about the opening. The lumina of the openings into the aneurysmal sac were almost completely occluded by an uneven mass of friable, yellowish-gray material, in appearance quite like the vegetations of bacterial endocarditis.

A microscopic section showed the wall of the artery and vein with much chronic inflammatory tissue between. A large channel lined with endothelium connected the two. This channel was filled with an irregular mass of thrombus which at one point showed some organization, but for the most part was fairly fresh. It was attached to the wall of the channel on both sides. Scattered through this thrombus were a great many polymorphonuclear cells and groups of large, rather poorly preserved, mononuclear cells filled with great swarms of Gram-positive cocci in short chains and surrounded by them (Fig. V). No bacteria were seen in the tissue.

Course of events after operation. After the wound had been dressed it was apparent that the circulation in the right leg was defective, for the skin was cold and mottled by areas of cyanosis. During the operation the leg had been elevated above the level of the heart. The patient was adjusted in the recovery bed so that the leg was held level with the heart and was surrounded with hot water bottles. At the end of an hour the circulation had improved greatly and the temperature of the skin had risen to a point a little above normal. The color of the skin was then a bright pink and the areas of cyanosis had disappeared. It is interesting to note what a profound effect even slight changes in hydrostatic pressure may have upon the circulation of an extremity when the circulation is impaired.

When the patient reached the ward the temperature was 96°, the pulse 160, respirations 48, blood pressure systolic 98, diastolic 74. During the afternoon the pulse rate fell to 130. The following day the patient was much better. The pulse rate varied from 120 to 140. The blood pressure had risen to systolic 128, diastolic 86. The color of the skin had changed gradually from a vivid pink to normal. For a few days there was a little edema of the right ankle, but this disappeared as the flushing of the skin subsided. It is possible that cutting the sympathetic nerve fibres about the wall of the external iliac artery may have caused temporary dilatation of the arterioles

in the right leg and in this way accounted for the bright pink color of the skin and the edema. We may assume that as vascular tone returned the color of the skin became normal and the edema disappeared. The variation in the temperature of the skin coincided with changes in color; when the skin was bright pink the temperature was elevated, as the skin assumed a normal appearance, the temperature returned to normal. Although the circulation in the right leg was

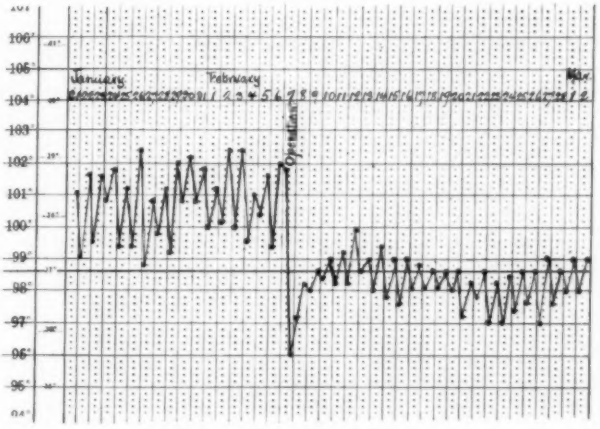

FIG. VI. CONDENSED TEMPERATURE CHART, SHOWING THE MAXIMUM AND MINIMUM TEMPERATURE EACH DAY BEFORE AND AFTER OPERATION

The temperature, varying from 99° to 102.4°, fell to subnormal on the day of operation and after a slight postoperative rise settled permanently to the normal level.

quite adequate to nourish the leg satisfactorily, still no pulsation could be felt in any of the arteries and the blood pressure could not be determined.

From then on the patient's recovery was uneventful. The temperature, as shown in the chart, fell to subnormal following the operation and thereafter never rose but a little above normal (Fig. VI). At the beginning of March he was out of bed in a chair and left the hospital in good condition on March 9, 1935. He had gained in weight. The blood count was at that time practically normal, namely,

hemoglobin 85 per cent.; red blood cells 4,400,000; leukocytes 6,600. The blood pressure in the arm was systolic 130, diastolic 95. The edge of the liver could still be felt at the costal margin on deep inspiration, but the spleen was no longer palpable. Blood cultures were taken two hours after the operation, again during the evening of the same day and on each of the succeeding six days. All of these cultures remained sterile.

Final report upon the patient. A letter from Dr. Caravati dated April 24, 1935, described the patient's condition as follows: "I am pleased to report that Mr. W. has steadily improved. He is walking about without help and gaining weight steadily. There remains a slight edema of the right foot. He has been constantly afebrile. His pulse now ranges from 75 to 85 beats to the minute. No pulsation has returned in the right leg. The liver and spleen are no longer palpable. His blood count is now practically normal. Two blood cultures have remained negative."

On May 31, 1935, the patient came to Baltimore for a final examination. He had gained forty pounds in weight, had an excellent color and was a picture of robust health. He had been working steadily for a month, at first for half a day but during the previous week for seven hours. He walked about without any support and complained only of a little pain in the leg if he walked too far. At the end of the day there was a little swelling about the ankle which disappeared during the night. The pulse rate was 76. The right leg was normal in appearance. The right thigh and calf measured 1 cm. more than the left. No pulsation could be felt in the right femoral artery nor in any other arteries of the leg.

RUPTURE OF A PAPILLARY MUSCLE IN THE HEART AS A CAUSE OF SUDDEN DEATH

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Rupture of a papillary muscle in the heart is not usually mentioned in the literature as one of the causes of sudden death (1), (2), (3). Only 19 cases have been reported, and the most complete paper on the subject lists but 11 examples. There are two cases in 6,000 autopsies at the Baltimore City Hospital, while not one is recorded either among 14,000 autopsies at the Johns Hopkins Hospital, or in the last 2000 autopsies performed at the University of Maryland Hospital.

The earliest case on record is that of Mérat (4), whose paper in 1803 has only once been given priority over that of Corvisart's of 1811 (5). Four more appeared in the French literature during the next century, but even as late as 1903, in the paper of Dévé (6), it is apparent that the true cause of the rupture was not recognized by the French. In 1887, Osler (7) stated that the coronary arteries were "much calcified" in a case which he reported, but Dennig (8), in 1909, was the first to stress the importance of coronary occlusion. Since his time, this has been recognized as the usual cause.

The coronary occlusion, as nearly as can be determined from the literature, has usually resulted from arteriosclerosis and thrombus formation. This was true of the case described here. When the anterior papillary muscle of the left ventricle is ruptured, occlusion of the anterior descending branch of the left coronary or of the first descending branch of the left circumflex is found. On the other hand, with rupture of the left posterior papillary muscle, occlusion of both the right coronary and the circumflex branch of the left has generally been found at autopsy.

While coronary occlusion will explain most of the cases described in the literature, there are apparently three exceptions. These are

the cases reported by Bertin (1824), Spanton (1865), and by Spalding and Von Glahn (1921).

Spalding and Von Glahn (9), reporting the first case seen at the Baltimore City Hospital, found no coronary occlusion, but stained treponema pallidum in the rupture ends of the papillary muscle. The two other cases, both showing rupture of a papillary muscle in the right ventricle, were similar in that extensive globular vegetations were found on the corresponding chordae tendineae. Bertin's patient (10) was a tuberculous girl of 22, while Spanton's was a 23 year old multipara dying with puerperal sepsis (11).

With the exception of the two cases mentioned above, the rupture in all reported cases has affected papillary muscles of the left ventricle. One of these involved both the anterior and the posterior muscles, ten involved the posterior alone, and only twice was the anterior muscle torn. Four of the earlier reports do not specify which muscle ruptured.

The clinical symptoms and signs in most of the cases described were those of acute coronary occlusion, but it is interesting that Boestrom, who saw the patient reported by Wankel (12), diagnosed "acute mitral insufficiency" from the murmurs heard over the heart, while the patient himself said that a muscle had broken in his heart. In several cases a systolic murmur has been heard at the apex of the heart. In three cases loud to-and-fro whistling sounds were heard over the precordium. In Spanton's case of rupture of a papillary muscle in the right ventricle, a loud systolic murmur was heard over the base of the heart.

Death occurred suddenly in nine of the cases reported in the literature. In one, life is said to have persisted for 20 months after the rupture. In Dennig's patient, who lived 10 months following the rupture, the torn ends of the muscle were smoothly covered with endocardium at autopsy (8).

In the following case death occurred suddenly and coronary occlusion was not suspected clinically.

CASE REPORT

History. C. T., colored woman, 52 years old. Admitted to the Baltimore. City Hospital 9/14/34. Died 10/16/34.

This patient was admitted on the Surgical Service to be treated for leg ulcers. Two days before death her blood pressure was 140/100. No other examination was recorded. About 7 A. M. on the day of death, while lying quietly on her bed, she developed sudden respiratory difficulty and lost consciousness. Death occurred within 15 minutes.

Autopsy No. 5829. Anatomical Diagnosis. Generalized arteriosclerosis and arteriolosclerosis; extreme sclerosis of cerebral and coronary arteries; thrombus in branch of left circumflex coronary; infarct in the myocardium; rupture of the left anterior papillary muscle; cardiac hypertrophy; chronic passive congestion; scars in the kidneys; cholelithiasis.

General. The body is that of an obese colored woman with ulcers on both legs. There is no peripheral edema, and no fluid is found in the serous cavities.

The heart weighs 530 grams. The coronary vessels stand out as very tortuous calcified tubes. The right coronary artery is diffusely sclerotic. No large projecting plaques are seen. The anterior descending and circumflex branches of the left are quite like the right, but the smaller branches are considerably narrowed. The first descending branch of the left circumflex shows even more sclerosis than other branches, and the small lumen which remains is completely occluded by a thrombus. In the left lateral and posterior walls of the left ventricle, about midway between the apex and base, there is a mottled red and yellow infarct, about 3.5 cm. long, extending from the endocardium to the epicardium. The anterior papillary muscle lies in this area, and it has a mottled yellow opaque appearance. It is ruptured at a point about 1 cm. below the attachment of the chordae tendineae (Fig. 1.). The broken ends are rough and show small hemorrhagic areas. The valves of the heart are practically normal.

Microscopical Note. There is extreme sclerosis of the coronary arteries. Calcium deposits and cholesterol crystals are abundant. Fresh thrombus material, partly organized, is seen completely occluding the lumen of the vessel as described above. In the myocardium of the left ventricle there are some old scars, and extensive areas of fresh necrosis with hemorrhage are found in the anterior papillary muscle and adjacent wall of the ventricle.

A brief summary of all previously recorded cases follows:

1. Mérat (4) 1803. *History.* Male, 44 years old. A wagoner who felt a cracking in his back while lifting a heavy cask. A feeling of suffocation developed, associated with violent palpitation. He was continuously bed-ridden until he died 20 months later. *Anatomical findings.* Rupture of one of columnae carneae to mitral valve. Aneurysm of aorta.

2. Corvisart (5) 1811. *History.* Male, 30 years old. A man of sedentary habits who had undertaken strenuous work. The onset of illness was 9 days before death, with hemoptysis and shortness of breath. Edema, irregular pulse, and restlessness developed. *Diagnosis:* Acute injury to heart; tearing in some part of it. *Anatomical findings.* Rupture of the muscle to the mitral valve. Fresh clot on torn ends of muscle. Heart not enlarged.

3. Bertin (10) 1824. *History.* Female, 22 years of age. Admitted to Cochin Hospital in last stages of phthisis, coughing severely. Died 18 hours after admission. *Anatomical findings.* Rupture of the papillary muscle of right ventricle. Vegetations on the chordae tendineae. Small heart.

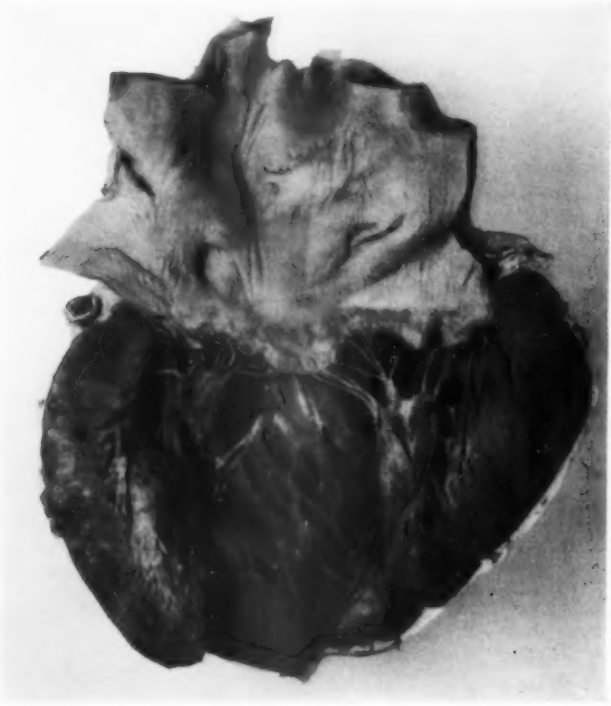

FIG. 1

4. Nicod (13) 1834. *History.* A woman of unknown age. She felt violent palpitations a fortnight before death, and was relieved by rest and two bleedings. The initial symptoms soon reappeared. A week later she had two more spells of suffocation. "The last carried her off." *Anatomical findings.* Rupture of both the papillary muscles in the left ventricle at a distance from one another. The torn extremities of different color explain the dates of the two spells of suffocation.

5. Spanton (11) 1865. *History.* Female, 23 years old. Died 7 weeks after

confinement, with peritonitis and pneumonia. Loud rough systolic murmur at base of heart. *Anatomical findings.* Rupture of one of the papillary muscles of the right ventricle. Firm vegetations on tricuspid valve and columnae carneae. Other valves healthy.

6. Le Pièz (14) 1873. *History.* A female of 74 years. She was suddenly taken with syncope. On return to consciousness complained of constriction of chest. "In a state of most pitiful anguish." Auscultation revealed murmurs and great irregularity of cardiac sounds. A week later the patient died suddenly. *Anatomical findings.* One of the papillary muscles of the left ventricle was severed, struck in two at the junction of the upper and middle third. Torn end caught between twisted chordae tendineae.

7. William Osler (7) 1887. *History.* A man of 70 years giving a history of long continued weakness. A systolic murmur was heard in the axilla. The pulse was irregular. *Anatomical findings.* Rupture of posterior papillary muscle of left ventricle. Calcified coronary arteries.

8. Dévé (6) 1908. *History.* Female, 77 years old. She had difficulty in breathing and weakness for 3 days before the appearance of sudden angina. Death occurred 45 minutes later. No murmurs were heard. *Anatomical findings.* Fresh rupture of posterior papillary muscle of the left ventricle. Coronary arteries free of all atheromatous change. No endocarditis.

9. Dennig (8) 1909. *History.* Male, 49 years old. There was a history of repeated angina with sudden onset of pain in left arm and tightness over precordium. Pneumonia, empyema, and pericarditis developed. He seemed to improve but was weak. Suddenly, on the 33rd day, when he awoke from sleep, he became nauseated, pulseless, and complained of a sensation of electricity in left arm. Cyanosis followed, and irregular precordial undulation. There were no murmurs. He died 7 hours after awakening. *Anatomical findings.* Rupture of posterior papillary muscle of the left ventricle. Torn end caught between twisted chordae tendineae. Extreme coronary sclerosis. Thrombus in right coronary artery. Large fatty heart.

10. Teacher (15) 1911. *History.* Male, 64 years old. The patient was a laboratory attendant at a hospital. He told friends a week before death that he was sure something was wrong with his heart. He was found unconscious, and died within 10 minutes. *Anatomical findings.* Rupture of papillary muscle of the left ventricle. Extreme coronary sclerosis. No thrombus found. Patchy infarction of papillary muscle.

11. Wankel (12) 1911. *History.* Male, 58 years old. Following a three year period of palpitation and shortness of breath, there was sudden onset of precordial pain, palpitation, and feeling of oppression. He told a physician something had torn in his heart. The heart was enlarged and a precordial heave was found associated with a very weak pulse. A loud systolic whistling sound was heard in diastole. The pulse became irregular, and pulmonary oedema developed. He died within 24 hours. *Diagnosis:*—Acute mitral insufficiency. *Anatomical findings.* Rupture of anterior papillary muscle of the left ventricle. Torn end

caught between twisted chordae tendineae. Sclerosis and thrombosis of first branch of left circumflex coronary artery. Heart enlarged.

12. Spalding and von Glahn (9) 1921. *History.* Male, 31 years old. He was a patient at the University of Maryland Hospital several months before death. The blood pressure was 130/50, and the Wassermann 4 plus. Typical signs of aortic insufficiency were present. He improved and was sent home, but later came to the Baltimore City Hospital. While being given admission tub-bath, he suddenly collapsed and died. *Anatomical findings.* Rupture of posterior papillary muscle of left ventricle. Torn ends covered by firmly adherent clot. Syphilitic aortitis. Fusion of aortic cusps. Rupture of left anterior cusp. Aortic insufficiency. Treponema pallidum in myocardium. Heart enlarged.

13. Fisher (16) 1922. *History.* Male, 62 years old. There was sudden onset of the signs and symptoms of acute cardiac insufficiency, associated with great pain. He was in a hospital for 10 months. A loud systolic-diastolic precordial murmur was heard and the pulse was very weak. *Anatomical findings.* Rupture of posterior papillary muscle of left ventricle. Torn end caught between twisted chordae tendineae, and smoothly covered by endocardium. Thrombi in the anterior descending branch of the left and distal end of the right coronary arteries.

14. Von Glahn and Horowitz (17) 1923. *History.* Female, 69 years old. While ironing, she suddenly developed symptoms of typical coronary occlusion. Cyanosis followed and the veins of her neck were full. The heart sounds were faint. A high pitched systolic murmur was heard over the precordium and in the left axilla. The heart beat was irregular and the B. P. was 100/70. Sudden hemiplegia developed and she died 21 days after onset. *Anatomical findings.* Rupture of posterior papillary muscle of left ventricle. Infarct in posterior wall of heart. Extreme coronary sclerosis. Thrombus in right circumflex artery.

15. Wagner (18) 1929. *History.* Male, 63 years old. There was onset of sudden pain in the left arm, followed three days later by a similar attack. The next day still another occurred. There was a loud apical diastolic murmur. Death occurred within 24 hours after the third attack of pain. *Anatomical findings.* Rupture of anterior papillary muscle of the left ventricle. Thrombus in the anterior descending branch of the left coronary artery near its origin. Heart enlarged.

16. Wagner (18) 1929. *History.* Male, 65 years old. Two days before death he began to have pain in the chest, increasing in severity. The heart beat was irregular and loud noises were heard over the precordium which had not been noted before. *Anatomical findings.* Rupture of posterior papillary muscle of the left ventricle. Sclerosis of coronary arteries. Thrombus in right coronary artery. Fresh infarct in myocardium.

17. Klein (19) 1929. *History.* Male, 58 years old. "Suffered for 2 years of affection of the heart." Two weeks before death he had an attack of violent substernal pain radiating to his back. While in bed the pulse ranged from 80–100, and the B.P. was 90/70. On the day of death he had a seizure of pain associated

with cold sweat and filiform pulse, and died 45 minutes later. *Anatomical findings.* Rupture of posterior papillary muscle of the left ventricle. Large foci of necrosis in the walls of left ventricle and in papillary muscle. Extreme coronary sclerosis. Thrombus in posterior descending branch of right coronary artery.

18. Jetzler and Finkeldey (20) 1931. *History.* Male, 58 years old. There was sudden onset of pain in the precordium, and 15 days later sudden shortness of breath occurred. The pulse was regular and full, but a to-and-fro loud noise was heard over the heart. He died 36 hours after the onset of last attack. *Anatomical findings.* Rupture of posterior papillary muscle of left ventricle. Foci of necrosis in anterior papillary muscle. Extreme coronary sclerosis. Thrombus in distal end of right coronary artery.

19. Voigt (21) 1932. *History.* Male, 59 years old. Three days before death sudden onset of pain in the whole chest. A feeling of apprehension, shortness of breath, and exhaustion developed. On the next day the pain localized in the left chest and epigastrium. On the day of death the pulse was slow and thready, and the apex beat was not palpable. A soft systolic apical murmur was heard, and the systolic blood pressure was low. The pulse became rapid and irregular before death. *Anatomical findings.* Rupture of posterior papillary muscle of left ventricle. Torn end caught between twisted chordae tendineae. Arteriosclerosis and narrowing of coronary arteries. Thrombus in circumflex branch of left coronary artery. Large infarct in posterior wall of left ventricle.

SUMMARY

Nineteen cases of rupture of a papillary muscle in the heart have been reported in the literature. These cases have been summarized, and one more has been described. The usual cause is coronary occlusion and infarction of the myocardium. Rupture of the left anterior papillary muscle is usually preceded by occlusion of either the anterior descending branch of the left coronary artery or of the first descending branch of the circumflex portion of the left coronary. Rupture of the left posterior papillary muscle is associated with occlusion of both the right artery and the circumflex branch of the left coronary artery.

Sudden death occurred in half of the cases which have been reported. The condition might be suggested clinically by the sudden onset of a loud whistling to-and-fro murmur occurring in association with the signs and symptoms of coronary occlusion and cardiac infarction.

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BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this journal.)

The Compleat Pediatrician. Practical, Diagnostic, Therapeutic—and Preventive Pediatrics. By WILBURT C. DAVISON. 1934. 1957 pp. and Index. *Duke University Press, Durham, N. C.*

Some years ago Dr. Davison published, under the title "Pediatric Notes", a compendium of therapeutic information—drugs, dosage, methods of fluid administration, feeding instructions, etc.—which proved exceedingly valuable. There one could find those bits of factual data which so frequently slip the mind at the moment of need, such as the exact number of drops of lactic acid for souring milk, or the method of preparing mercurochrome for intravenous use. I know of one recent medical graduate who practiced a high grade of pediatrics in the wilds of Labrador for an entire year with this slim volume as his only guide.

There has appeared recently from the Duke University Press a second volume by the same author, larger in its scope than the original. This book attempts not only to tabulate therapeutic measures, but to intercalate symptoms and signs in such a way that diagnosis becomes very nearly automatic. Thus, in Chapter I, under the heading of *Cough* there appear thirty-seven possible causes for this symptom, with numerals behind each denoting the paragraph in Chapter II devoted to a short summary of that disease. In this summary figures after each symptom refer back to paragraphs in Chapter I, so that ultimately, after scrambling back and forth from paragraph to paragraph, one either arrives at the diagnosis or achieves, as I did, a state of acute dizziness. The disease summaries are occasionally so incomplete as to be incorrect; *e.g.*, "abscess, retroperitoneal; symptoms and signs:—Fever, abdominal pain, enlargement or tumors." Surely the almost invariable limp and flexion deformity of the thigh deserve places in the picture. Again one is told that the murmur of patent ductus arteriosus is always systolic and diastolic, and there are numerous other errors of omission as well as commission.

Chapters III, IV, V, VI, and VII are devoted to Preventive Measures, Fluid Administration, Diet, Drugs, and Laboratory Procedures, and are complete and exceedingly useful. Much that appeared in "Pediatric Notes" has been revised and brought up-to-date, and much new material has been added.

In short, the book can be recommended highly for the virtues of its last five chapters; the enormous amount of time and labor consumed in the laborious compilation of Chapters I and II can only be regretted; and the whimsical touch in adapting the frontispiece of "The Compleat Angler" for the volume can be overlooked. The balance is distinctly favorable.

A. J. S.

Surgical Pathology of the Peritoneum. By ARTHUR E. HERTZLER. 1935. 304 pp. 201 illust. *J. P. Lippincott Co.*, (1) *Phila., Pa.*

Already a prolific author, Arthur E. Hertzler, announces with the presentation of this volume another on the Surgical Pathology of the Gastro-intestinal tract in preparation with three other monographs to follow, namely, the surgical pathological diseases of the neck, mouth and jaw and of the thyroid gland.

In his preface Dr. Hertzler pays high tribute to the drawings of Tom Jones and the photographs of Barlow, and without any question the illustrations are of great value. They are both numerous and well executed. The monograph is logically developed, starting with an excellent chapter on the anatomy of the peritoneum followed by the pathology. One of the most helpful chapters is the one on peritoneal adhesions, a question that vexes the most skilful surgeon. The chapters on the acute peritoneum are excellently presented and give in detail the pathology which the surgeon observes as he operates. This is exceedingly helpful to the reader in his daily work at the operating table. Other chapters on the omentum, blood vessels and tumors of the peritoneum are of great value to the operating surgeon. An informal and somewhat unusual bibliography is given at the close of each chapter. We shall look forward to the completion of Dr. Hertzler's other monographs on surgical pathology.

G. A. S.

A History of Embryology. By JOSEPH NEEDHAM. 1934. 274 pp. Illust. $4.00. *University Press, Cambridge; Macmillan Co., New York.*)

In four chapters dealing with antiquity, the middle-ages and the Renaissance, the 17th and the 18th centuries, the author covers the entire history of Embryology up to the year 1814. The scholarly way in which the subject is treated, the excellent illustrations and the extensive bibliography will make this book a most valuable help to the historian and fascinating reading to every biologist. It is therefore sincerely to be hoped that Dr. Needham will soon publish the second volume which together with the present one will give the first exhaustive history of embryology from ancient down to modern times.

O. T.

The Physician's Art. An Attempt to expand John Locke's Fragment *De Arte Medica.* By ALEXANDER GEORGE GIBSON. 1933. 237 pp. $3.00. (*The Clarendon Press, Oxford.*)

The first chapter of this book is devoted to an historical introduction to John Locke's *De arte medica* together with a reprint of this fragment which was written in 1669. The entire remainder of the work is an exposition of "what appear to the author the fundamentals of the medical art" treated under the various aspects of "art and science," diagnosis, prognosis, etc. Dr. Gibson's opinions are never dogmatic; they are marked by a sound knowledge of ancient writers, by good common-sense and above all, by a sincere devotion to the work of the practitioner.

O. T.

Treatment by Diet. By CLIFFORD J. BARBORKA, B.S., M.S., M.D., D.Sc., F.A.C.P. Northwestern University Medical School. xii + 615 pp. 7 figs. 14.5 x 22.5 cm. (*J. B. Lippincott Co., Philadelphia, 1935.*)

In the treatment of his subject the author has adhered rigidly to the fundamental principles and widely accepted ideas in the field of nutrition. Thereby he has excluded the fads, vagaries, and folk-lore that have so long created false impressions and have obscured the true value of nutritive measures in therapeutics. By separating diseases in which diet is the principal armamentarium of the physician from those in which diet is of questionable aid, he has indicated the limitations and at the same time the valuable but selective efficacy of nutrition in combating disease.

The book consists of three parts. The first, entitled *Diet in Health*, deals with the essential constituents of a diet and lists typical menus for the normal adult. In the case of the vitamins, a series of charts indicate their functions, their distribution in foodstuffs, and the clinical manifestations consequent upon a deficiency of them.

In the second part, *Application of Dietotherapy*, the mathematics of calorie calculation, so uninspiring and repugnant to many minds, is painlessly camouflaged in the form of "servings." But whether in "servings" or in "shares," as foodstuffs are now so commonly visualized, he who would use the book effectively must still count the calories.

The third part, *Diet in Disease*, is divided into two sections: (a) diseases in which diet is of paramount importance, such as diabetes mellitus, gout, overweight, underweight, nephritis, pernicious anemia, peptic ulcer, constipation, and the deficiency diseases; and (b) conditions in which diet is of varying importance, such as febrile diseases, the gamut of gastro-intestinal disorders, urinary and skin maladies.

The author discusses the leading theories of dietary control of diabetes with the recommendation of a plan intermediate between the extreme views. He devotes 28 pages to the problem of overweight and 10 pages to underweight. With one-half the population seeking to reduce, and the other half to gain weight, it behooves the physician to know the approved methods. Control of constipation by diet, a measure that has never been explored to the fullest extent by physicians, is given 23 pages.

In the section on diseases in which diet is of varying importance, we find to a large extent those conditions for which menus are detailed on a legendary rather than on a scientific basis. That the author has frankly admitted the doubtful results, if not the rationale, of diet in this class of disorders is a distinctly forward step that may serve to induce investigation in this field.

Not the least commendatory feature of the book is the helpful bibliography, in which the author has shown exemplary courtesy in mentioning rival texts.

The modern physician should certainly be well versed in the dietary treatment of disease. Dr. Barborka's book will furnish all the information that the practitioner needs.

H. D. K.